10/523,111 Page 3

chain bonds :

2-12 7-13 10-14 18-20 19-21

ring bonds :

1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 9-10 10-11 11-12 14-15 14-19

15-16 16-17 17-18 18-19

exact/norm bonds :

1-2 1-6 2-3 2-12 3-4 4-5 5-6 7-8 7-12 7-13 8-9 9-10 10-11 11-12

exact bonds :

10-14 18-20 19-21

normalized bonds :

14-15 14-19 15-16 16-17 17-18 18-19

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:Atom 12:Atom 13:CLASS 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom

20:CLASS 21:CLASS

L1 STRUCTURE UPLOADED

0

=> d 11

L1 HAS NO ANSWERS

L1 STR

rings not isolated

12 ANSWERS

Structure attributes must be viewed using STN Express query preparation.

=> s l1

Habte

SAMPLE SEARCH INITIATED 10:11:25 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 128 TO ITERATE

100.0% PROCESSED SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**

128 ITERATIONS

BATCH **COMPLETE**

PROJECTED ITERATIONS: 1882 TO 3238

PROJECTED ANSWERS: 33 TO 447

L2 12 SEA SSS SAM L1

02/09/2007

10/523,111 Page 4

=> s l1 sss full FULL SEARCH INITIATED 10:11:31 FILE 'REGISTRY' FULL SCREEN SEARCH COMPLETED - 2760 TO ITERATE

100.0% PROCESSED 2760 ITERATIONS 241 ANSWERS

SEARCH TIME: 00.00.01

L3 241 SEA SSS FUL L1

=> file caplus

COST IN U.S. DOLLARS SINCE FILE TOTAL ENTRY SESSION 172.10 172.31

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=> s 13

L4 22 L3

=> d ibib abs hitstr tot

L4 ANSWER 1 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:
DOCUMENT NUMBER:
143:229869
Preparation of phthalazinone derivatives as PDE4 inhibitors
INVENTOR(S):
Hatzelmann, Armin; Barsig, Johannes; Marx, Degenhard; Kley, Hans-Peter; Christians, Johannes A. M.; Menge, Wiro M. P. B.; Sterk, Geert Jan

PATENT ASSIGNEE(S):
SOURCE:
POCUMENT TYPE:
DOCUMENT TYPE:
LANGUAGE:
PATENT ASSIGNEE(S):
SOURCE:
PATENT ASSIGNEE(S):
Altana Pharma A.-G., Germany
PCT Int. Appl., 57 pp.
CODEN: PIXXD2
PATENT TYPE:
English

English

DOCUMENT TYPE: LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE WO 2005075457 WO 2005075457 20050818 WO 2005-EP50417 20050201 A1 A8 20060302 AB 20050302
AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, EM, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, 1D, IL, IN, IS, JP, KE, KG, KP, KR, KZ, CL, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MM, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SV, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZM, SM

RW: BN, GH, GM, KE, LS, MN, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZM, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, PI, PR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BP, BJ, CP, CG, C1, CM, GA, GN, GG, GM, ML, MR, NE, SN, TD, TG

EP 1720854

R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, PI, PR, GB, GR, HU, IE, IS, IT, LI, LI, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR

PRIORITY APPLN. INFO:

EP 2004-2423

A 20040204

WO 2005-EP50417 W 20050201

OTHER SOURCE(S): MARPAT 143:229869

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [R1 and R2 are both H or together from an addnl. bond; R3 = (un)substituted phenyl; R4 = OH, alkoxy, NHR5, etc.; R5 = OH, alkoxy or alkoxyalkyl; n = 0, 2, 3, or 4) and their pharmaceutically acceptable salts, are prepared and disclosed as PDR4 inhibitors. Thus, e.g., II was prepared by coupling of (485,88R)-4-(3,4-dimethoxy-phenyl)-2-piperidin-4-yl-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one hydrochloride (preparation given) with

ANSWER 1 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

862462-50-8 CAPLUS
Piperazine, 1-[4-[4-[4-[(4a5,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]-1,4-dioxobutyl]-4-methyl-, (2E)-2-butenedioate (9CI) (CA INDEX NAME)

CM 1

CRN 862462-49-5 CMF C30 H41 N5 O5

Absolute stereochemistry.

CRN 110-17-8

Habte

ANSWER 1 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued) different methods utilizing cAMP and it was revealed that compds of the invention displayed -logICSO values in the range of 8.4 up to 10.4 mol/L. I as inhibitor of PDE4 should prove useful in the treatment of airway disorders. Pharmaceutical compns. comprising I are disclosed. 852462-47-3P RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses) (preparation of phthalazinone derivs. as PDE4 inhibitors) 852462-47-3 CAPLUS 1-Piperidinebutanoic acid, (485,881-4-(3,4-dimethoxyphenyl)-4a,5,8,8ateterahydro-1-oxo-2(1H)-phthalazinyl)-y-oxo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

862462-48-4P 862462-50-8P 862462-51-9P
852462-53-1P 852462-54-2P 862462-55-3P
852462-56-4P 862462-55-5P 862462-58-6P
852462-59-7P 862462-60-0P 862462-61-1P
852462-62-2P 862462-63-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of phthalazinone derivs. as PDE4 inhibitors)
852462-48-4 CAPLUS
Morpholine, 4-[4-[4-[(48S,88R)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]-1,4-dioxobutyl]-

Absolute stereochemistry.

ANSWER 1 OF 22 CAPLUS COPYRIGHT 2007 ACS ON STN CMP C4 H4 O4

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862462-51-9 CAPLUS
1-Piperidinebutanamide, 4-{(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl}-γ-oxo-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

862462-53-1 CAPLUS
Piperazine, 1-[4-[4-[4-[(4a5,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl}-1,4-dioxobutyl]-4-[2-(2-oxo-1-pyrrolidinyl)ethyl]-, (2E)-2-butenedioate [9CI] (CA INDEX NAME)

CRN 862462-52-0 CMF C35 H48 N6 O6

L4 ANSWER 1 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

(Continued)

CRN 110-17-8 CMF C4 H4 O4

Double bond geometry as shown.

% 862462-54-2 CAPLUS 1-Piperidineacetamide, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]- α -oxo-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 1 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

Absolute stereochemistry.

862462-57-5 CAPLUS
1-Piperidineacetamide, 4-[{4as,8aR}-4-(3,4-dimethoxyphenyl}-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl}-N,N-dimethyl-q-oxo-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

862462-58-6 CAPLUS 1-Piperidineacetamide, 4-{(4as,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl}-N-hydroxy- α -oxo-(9CI) (CA INDEX INDEX

Absolute stereochemistry.

L4 ANSWER 1 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 862462-55-3 CAPLUS .
CN Morpholine.
1-0x0-2(1H)-phthalazinyl]-1-piperidinyl]oxoacetyl]- (9CI) (CA INDEX NAME)

 ${\bf Absolute \ stereochemistry}.$

RN 862462-56-4 CAPLUS
Piperazine,
1-[[4-[(48,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]oxoacetyl]-4-methyl-,
monohydrochloride (9CI) (CA INDEX NAME)

L4 ANSWER 1 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 862462-59-7 CAPLUS
CN 1-Piperidineacetamide,
4-{{4as,8aR}-4-{3,4-dimethoxyphenyl}-4a,5,6,7,8,8a-hexahydro-1-oxo-2(1H)-phthalazinyl}-a-oxo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

862462-60-0 CAPLUS
Morpholine, 4-[4-[4-[4as,8aR]-4-(3,4-dimethoxyphenyl]-4a,5,6,7,8,8a-hexahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]oxoacetyl]- (9CI) (CA INDEX NAME)

L4 ANSWER 1 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

862462-61-1 CAPLUS
Piperazine, 1-[{4-{(4a5,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,6,7,8,8a-hexahydro-1-0x0-2(1H)-phthalazinyl]-1-piperidinyl]oxoacetyl]-4-methyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

862462-62-2 CAPLUS 1-Piperidineacetic acid, 4-[{4aS,8aR}-4-(3,4-dimethoxypheny1}-4a,5,8,8a-tetrahydro-1-oxo-2(1R)-phthalaziny1}- α -oxo-, 2,2-dimethylhydrazide (9CI) (CA INDEX NAME)

ANSMER 1 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued) 1(2H)-Phthalezinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8-tetrahydro-2-(4-piperidinyl)-, monohydrochloride, (4ds, 8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

785047-47-4 CAPLUS 1(2H)-Phthalazinone, ,4-dimethoxyphenyl)-4a,5,6,7,8,8a-hexahydro-2-(4-piperidinyl)-, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

862462-64-4 CAPLUS
1-Piperidineacetic acid, 4-[(485.88R)-4-(3,4-dimethoxyphenyl)-48,5,8,8s-tetrahydro-1-oxo-2(1H)-phthalazinyl]-a-oxo-, methyl ester (9CI) (CA INDEX MAME)

Absolute stereochemistry.

Habte

L4 ANSWER 1 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN Absolute stereochemistry. (Continued)

862462-63-3 CAPLUS
1-Piperidineacetamide, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-(2-methoxyethyl)-a-oxo- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

380226-97-1P 785047-47-4P 862462-64-4P 862462-65-5P RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation of phthalazinone derivs. as PDE4 inhibitors) 380226-37-1 CAPLUS

ANSWER 1 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

862462-65-5 CAPLUS 1-Piperidineacetic acid, 4-{(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4.5,6.7,8.8a-hexahydro-1-oxo-2(1H)-phthalazinyl]- α -oxo-, methylester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

REFERENCE COUNT: FORMAT

THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

02/09/2007

L4 ANSWER 2 OF 22 CAPLUS COPYRIGHT 2007 ACS ON STN ACCESSION NUMBER: 2005:823688 CAPLUS CAPLUS 143:229868 Prepare: 48

Preparation of piperidinyl pyridazinone derivatives

PDE4 inhibitors

PDEW inhibitors
Hatzelmann, Armin; Barsig, Johannes; Marx, Degenhard;
Kley, Hans-Peter; Christiaans, Johannes A. M.; Menge,
Wiro M. P. B.; Sterk, Geert Jan
Altana Pharma A.-G., Germany
PCT Int. Appl., 53 pp.
CODEN: PIXXD2
Patent
English
1 INVENTOR(S):

PATENT ASSIGNEE(S): SOURCE:

DOCUMENT TYPE: LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

PATEN	r 1	NFOR	MATI	ON:														
PATENT NO.																		
1	WO 2005075456			A1 200			50818 WO 2005-EP50415					415	20050201					
1	WO 2005075456			AB		2006	0302											
		W:	AE,	AG,	AL,	AM,	AT,	AU,	AZ,	BA,	BB,	BG,	BR,	BW,	BY,	ΒZ,	CA,	CH,
			CN,	co,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	EG,	ES,	FI,	GB,	GD,
			GE,	GH,	GM,	HR,	HU,	ID,	IL,	IN,	IS.	JP,	KE,	KG,	KP,	KR,	KZ,	LC,
			LK.	LR,	LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NA,	NI,
			NO.	NZ,	OM,	PG,	PH,	PL,	PT,	RO,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	SY,
			TJ.	TM,	TN,	TR,	TT,	TZ,	UA,	UG,	US,	UZ,	VC,	VN,	YU,	ZA,	ZM,	ZW,
SM																		
		RW:	BW.	GH,	GM.	KE,	LS,	MW,	MZ,	NA,	SD.	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,
			AZ,	BY,	KG,	KŹ,	MD,	RU,	TJ,	TM,	AT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,
			EE.	ES.	FI.	FR,	GB,	GR,	HU,	IE,	IS,	IT,	LT,	LU,	MC,	NL,	PL,	PT,
			RO.	SE.	SI.	SK.	TR,	BF,	BJ,	CF,	CG,	CI,	CM,	GA,	GN,	GQ,	GW.	ML,
			MR.	NE,	SN.	TD.	TG											
,	AU 2005210042							2005	0818	1	AU 20	005-	2100	20050201				
	CA 2554797							2005	0818		CA 20	005-	2554	797		21	0050	201
	EP 1716133				A1		2006	1102	1	EP 20	005-	7166	09					
								ES,										
								CY,										
PRIORITY APPLN. INFO.:								,							,			204

WO 2005-EP50415 W 20050201

OTHER SOURCE(S):

MARPAT 143:229868

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Title compds. I [R1 and R2 independently = alkyl; R3 = (un)substituted phenyl; R4 = COR5, S(0)2R6(CH2)nCOR7 or CO(CH2)mR8; R5 = alkyl, NR9R10 or (un)substituted phenyl; R6 = alkyl, NR1R12 or (un)substituted phenyl; R7 = NR13R14; R8 = NR15R16; R9-16 independently = H, alkyl, cycloalkyl,

etc.; $n = 1-4; \; m = 1-4 \} \; \text{and their pharmaceutically acceptable salts, are prepared}$

ANSWER 2 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

●x HCl

RN 862578-20-9 CAPLUS
CN 1-Piperidineacetamide,
4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-6-oxo-1(4H)pyridazinyl]-(9C1) (CA INDEX NAME)

Habte

862578-31-0 CAPLUS
Piperidine, 4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-5,5-dimethyl-6-oxo1(4H)-pyridazinyl)-1-[(2,5-dioxo-1-pyrrolidinyl)acetyll- (9C1) (CA INDEX

RN 862578-22-1 CAPLUS
CN Piperidine, 4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-5,5-dimethyl-6-oxo-

ANSWER 2 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued) and disclosed as PDE4 inhibitors. Thus, e.g., II was prepd. by coupling of 6-(3,4-dimethoxyphenyl)-4,4-dimethyl-2-piperidin-4-yl-4,5-dihydro-2H-pyridazin-3-one (prepn. given) with 3-cyanobenzenesulfonyl chloride. The inhibitory activity of I was evaluated using scintillation proximity

Inhibitory activity of 1 was evaluated using scintilation proximity y and it was revealed that selected compds. of the invention displayed logics values in the range of 7.60 up to 9.68 mol/L. I as inhibitor of PDEA should prove useful in the treatment of airway disorders.

Pharmaceutical compns. comprising I are disclosed.

862578-18-5P 862578-19-6P 862578-20-9P 862578-31-0P 862578-31-0P 862578-32-9P 862578-32-9P 862578-32-9P 862578-32-9P 862578-32-9P 862578-32-9P 862578-33-1P 862578-32-9P 862578-33-4P 862578-32-9P 862578-33-4P 862578-32-9P 862578-32-9P 862578-33-9P 862578-33-9P 862578-39-0P RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(Uses)
(preparation of piperidinyl pyridazinone derivs. as PDE4 inhibitors)
863578-18-5 CAPLUS
Piperidine, 1-((2-cyanophenyl)sulfonyl)-4-(3-(3,4-dimethoxyphenyl)-5,6-dihydro-5,5-dimethyl-6-oxo-1(4H)-pyridazinyl)- (9C1) (CA INDEX NAME)

862578-19-6 CAPLUS
Morpholine, 4-[3-[4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-5,5-dimethyl-6-oxo-1(4H)-pyridazinyl]-1-piperidinyl]-1-oxopropyl]-, hydrochloride (9CI) (CA INDEX NAME)

ANSWER 2 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued) 1(4H)-pyridazinyl]-1-{(2-methylphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

862578-24-3 CAPLUS
Piperidine, 1-[(4-cyanophenyl)sulfonyl]-4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-5,5-dimethyl-6-oxo-1(4H)-pyridazinyl]- (9CI) (CA INDEX NAME)

862578-25-4 CAPLUS
Piperidine, 4-[3-{3,4-dimethoxyphenyl}-5,6-dihydro-5,5-dimethyl-6-oxo-1(4H)-pyridazinyl]-1-[{2-(trifluoromethoxy)phenyl]sulfonyl}- (9CI) (CA INDEX NAME)

862578-26-5 CAPLUS
Piperidine, 4-(3-(3,4-dimethoxyphenyl)-5,6-dihydro-5,5-dimethyl-6-oxo-1(4H)-pyridazinyl)-1-(2-methoxybenzoyl)- (9Cl) (CA INDEX NAME)

02/09/2007

L4 ANSWER 2 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 862578-27-6 CAPLUS
CN Piperidine, 1-[(3-cyanophenyl)sulfonyl]-4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-5,5-dimethyl-6-oxo-1(4H)-pyridazinyl}- (9CI) (CA INDEX NAME)

RN 862578-28-7 CAPLUS
CN Piperidine, 4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-5,5-dimethyl-6-oxo-1(4H)-pyridazinyl]-1-[(4-methylphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 862578-29-8 CAPLUS
CN Piperidine, 4-[3-43,4-dimethoxyphenyl)-5,6-dihydro-5,5-dimethyl-6-oxo1(4H)-pyridazinyl)-1-[(3-methylphenyl)sulfonyl)- (9CI) (CA INDEX RAME)

L4 ANSWER 2 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Cont

RN 862578-30-1 CAPLUS
CN 1-Piperidinesulfonamide, 4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-5,5-dimethyl-6-oxo-1(4H)-pyridazinyl]-N,N-dimethyl- (9CI) (CA INDEX NAME)

RN 862578-31-2 CAPLUS
CN 1-Piperidineacetamide, 4-[3-{2,3-dihydro-7-methoxy-2,2-dimethyl-4-benzofuranyl)-5,6-dihydro-5,5-dimethyl-6-oxo-1(4H)-pyridazinyl]- (9CI) (CA INDEX NAME)

L4 ANSWER 2 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 862578-32-3 CAPLUS CN Piperidine, 1-benzoyl-4-(3-(3,4-dimethoxyphenyl)-5,6-dihydro-5,5-dimethyl-6-oxo-1(4H)-pyridazinyl]- (9CI) (CA INDEX NAME)

RN 862578-33-4 CAPLUS
CN 1-Piperidineacetamide,
4-[3-(3,4-dimethoxyphenyl)-5,5-diethyl-5,6-dihydro6-0X0-1(4H)-pyridazinyl)-, hydrochloride (9CI) (CA INDEX NAME)

L4 ANSWER 2 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

•x HCl

RN 862578-34-5 CAPLUS
CN Piperidine, 1-((2-cyanophenyl)sulfonyl)-4-(3-(3,4-dimethoxyphenyl)-5,5-diethyl-5,6-dihyl-5-6-oxo-1(4H)-pyridazinyl)- (9CI) (CA INDEX RAME)

RN 862578-35-6 CAPLUS
CN Piperidine, 4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-5,5-dimethyl-6-oxo-1(4H)-pyridazinyl]-1-[(3,5-dioxo-4-morpholinyl)acetyl]- (9CI) (CA INDEX NAME)

RN 862578-36-7 CAPLUS CN Piperidine, 02/09/2007 dimethoxyphenyl)-5,5-diethyl-5,6-dihydro-6-oxo-1(4H)-

Habte

10/523,111

Page 10

ANSWER 2 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued) pyridazinyl]-1-(2-methoxybenzoyl)- (9CI) (CA INDEX NAME)

862578-37-8 CAPLUS
Piperidine, 4-[3-(2,3-dihydro-7-methoxy-2,2-dimethyl-4-benzofuranyl)-5,6-dihydro-5,5-dimethyl-6-oxo-1(4H)-pyridazinyl]-1-[(4-methyl-1-piperazinyl)acetyl]- (9CI) (CA INDEX NAME)

862578-38-9 CAPLUS
Piperidine, 4-[3-(2,3-dihydro-7-methoxy-2,2-dimethyl-4-benzofuranyl)-5,6-dihydro-5,5-dimethyl-6-oxo-1(4H)-pyridazinyl]-1-{(2,5-dioxo-1-pyrrolidinyl)acetyl)- (9CI) (CA INDEX NAME)

L4 ANSWER 2 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

(Continued)

862578-39-0 CAPLUS
Piperidine, 1-{(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)acetyl}-4-{3-(3,4-dimethoxyphenyl)-5,6-dihydro-5,5-dimethyl-6-oxo-1(4H)-pyridazinyl]-(9CI)
(CA INDEX NAME)

IT 862578-44-7P 862578-48-1P 862578-54-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of piperidinyl pyridazinone derivs. as PDE4 inhibitors)
RN 862578-44-7 CAPLUS
CN 3(2H)-Pyridazinone
6-(3,4-dimethoxyphenyl)-4,5-dihydro-4,4-dimethyl-2-(4-piperidinyl)- (9CI) (CA INDEX NAME)

L4 ANSWER 2 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

L4 ANSWER 2 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

862578-48-1 CAPLUS
3(2H)-Pyridazinone,
,3-dihydro-7-methoxy-2,2-dimethyl-4-benzofuranyl)4,5-dihydro-4,4-dimethyl-2-(4-piperidinyl)-, hydrochloride (9CI) (CA
INDEX NAME)

●x HCl

862578-54-9 CAPLUS
3(2H)-Pyridazinone, 6-(3,4-dimethoxyphenyl)-4,4-diethyl-4,5-dihydro-2-(4-piperidinyl)-, hydrochloride (9Cl) (CA INDEX NAME)

●x HCl

THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

(Continued)

L4 ANSWER 3 OF 22 CAPLUS COPYRIGHT 2007 ACS ON STN ACCESSION NUMBER: 2005:232615 CAPLUS COPYRIGHT 2007 ACS ON STN 142:291403 Use of Page 142:291403 142:291403
Use of phosphodicaterase 4 (PDB4) inhibitors for the treatment of diabetes mellitus
Hauser, Daniels; Hansuer, Guido; Grundler, Gerhard;
Schmidt, Beate; Kemkowski, Joerg; Kley, Hans-Peter
Altana Pharma A.-G., Germany
PCT Int. Appl., 50 pp.
CODEN: PIXXD2

INVENTOR(S):

PATENT ASSIGNEE(S): SOURCE:

DOCUMENT TYPE: English

FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

	•••	INF OR		J14 :														
PATENT NO.											DATE							
							-									-		
	WO	2005	0232	53		A1		2005	0317	1	WO 2	004 -	EP52	005		2	0040	902
	WO	2005	0232	53		A8		2006	0302									
		W:	ΑE,	AG,	AL,	AM,	AT,	ΑU,	AZ,	BA,	₿B,	BG,	BR,	BW,	BY,	ΒZ,	CA,	CH,
			CN,	co,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	EG,	ES,	FI,	GB,	GD,
			GE,	GH,	GM,	HR,	ΗU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	KP,	KR,	KZ,	LC,
			LK,	LR,	LS,	LT.	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NA,	NI,
			NO.	NZ,	OM,	PG,	PH,	PL.	PT,	RO,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	SY,
			TJ.	TM.	TN.	TR,	TT,	TZ,	UA,	UG,	US,	UZ,	VC,	VN,	YU,	ZA,	ZM,	ZW
,		RW:	BW,	GH,	GM.	KE,	LS,	MW,	MZ,	NA,	SD,	SL,	52,	TZ,	UG,	ZM,	ZW.	AM,
			AZ.	BY,	KG.	KZ,	MD,	RU,	TJ,	TM,	AT,	BE.	BG,	CH.	CY,	cz,	DE.	DK,
			EE.	ES.	FI.	FR,	GB,	GR,	HU,	IE.	IT.	LU,	MC.	NL.	PL,	PT,	RO.	SE,
			SI.	SK.	TR.	BP.	BJ.	CF.	CG.	CI.	CM,	GA,	GN,	GQ.	GW,	ML,	MR.	NE.
			SN.	TD.	TG													
	ΑU	2004	2699	23		A2		2005	0317		AU 2	004 -	2699	23		2	0040	902
	ΑU	2004	2699	23		A1		2005	0317									
		2537						2005	0317		CA 2	004-	2537	230		2	0040	902
	US	2006	2817	45		Al		2006	1214		US 2	006-	5706	22		2	0060	303
10		APP										003-						

WO 2004-EP52005

W 20040902

W0 2004-EP\$2005 W 20040902

The invention discloses the use of certain known PDE4 inhibitors for the treatment of disbetes mellitus and accompanying disorders thereof. 449760-14-9 449760-15-0 449760-16-1 449760-17-2 449760-19-4 449760-20-7 449760-20-19-4 49760-20-7 449760-21-8 449760-22-9 449760-26-3 449760-28-5 449760-25-2 449760-26-3 449760-28-5 449760-30-9 449760-35-4 449760-40-1 449760-49-0 449760-35-4 449760-51-4 449760-51-6 4497

RN 449760-14-9 CAPLUS CN Piperidine, 4-[(4eS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-

L4 ANSWER 3 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN Absolute stereochemistry.

RN 449760-17-2 CAPLUS
CN 1-Piperidinepentanoic acid,
4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8atetrahydro-1-oxo-2(1H)-phthalazinyl]-5-oxo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

449760-19-4 CAPLUS
1-Piperidinecarboxamide, 4-[(4a5,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-(1,1-dimethylethyl)- (9CI) (CA INDEX RAME)

Absolute stereochemistry.

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ANSWER 3 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued) 2(1H)-phthalazinyl]-1-[(4-methylphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-15-0 CAPLUS CN Piperidine, 4-{{4a5,8aR}-4-{3,4-diethoxyphenyl}-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl}-1-(methylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

449760-16-1 CAPLUS
Piperidine, 1-acetyl-4-{(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl)- (9CI) (CA INDEX NAME)

ANSWER 3 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

449760-20-7 CAPLUS

1-Piperidinecarboxamide, 4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

449760-21-8 CAPLUS
1-Piperidinecarboxamide, 4-[(4aS,8aR]-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-(1,1-dimethylethyl)- (9CI) (CA

L4 ANSWER 3 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

449760-22-9 CAPLUS 1-Piperidinecarboxamide, 4-[(4aR,8aS)-4-(2,3-dihydro-7-methoxy-2,2-

dimethyl-4-benzofuranyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-(1,1-dimethylethyl)-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

449760-23-0 CAPLUS
Piperidine, 4-[(4as,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1cox-2(1H)-phthalazinyl]-1-[[5-(dimethylamino)-1-naphthalenyl]sulfonyl](9CI) (CA INDEX NAME)

Absolute stereochemistry.

ANSWER 3 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 449760-25-2 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(4pyridinylmethyl)-4-piperidinyl]-, (4a5,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-26-3 CAPLUS
CN Morpholine,
4-[[4-[[4-2]] A-dimethoxyphenyl] -4a,5,8,8a-tetrahydro1-oxo-2(lH)-phthalazinyl] -1-piperidinyl|carbonyl] - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 3 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

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RN 449760-24-1 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(4-nitrophenyl)-4-piperidinyl]-, (4eS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 3 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 449760-28-5 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(1methyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)-4-piperidinyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

L4 ANSWER 3 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

(Continued) PAGE 2-A

449760-29-6 CAPLUS
1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4e,5,8,8a-tetrahydro-2-(1-thieno[2,3-d)pyrimidin-4-yl-4-piperidinyl)-, (4aS,8aR)- (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 2-A

RN 449760-30-9 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-{2-

ANSWER 3 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN NAME) (Continued)

Absolute stereochemistry.

449760-42-3 CAPLUS
2,3-Piperazinedione, 1-[[4-[[48S,88R]-4-[3,4-dimethoxyphenyl]-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]carbonyl]-4-ethyl-(SCI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-47-8 CAPLUS
CN Piperidine,
4-[(445,84R)-4-(1,4-diethoxyphenyl)-48,5,8,8a-tetrahydro-1-oxo2(1H)-phthalazinyl)-1-(4-pyridinylcarbonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

ANSWER 3 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued) pyrimidinyl)-4-piperidinyl]-, (4as,8ar)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-35-4 CAPLUS
CN Morpholine,
4-[[4-[[48.5aR]-4-(3,4-diethoxyphenyl]-4a,5,8,8a-tetrahydro-1oxo-2(1H)-phthalazinyl]-1-piperidinyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

449760-40-1 CAPLUS
1-Piperidineacetamide, 4-[(4as,8am)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-(1-methylethyl)- (9CI) (CA INDEX

ANSWER 3 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

449760-48-9 CAPLUS 1(2H)-Phthalezinone, 2-{1-(2-(4-amino-3,5-dichlorophenyl)-2-oxoethyl)-4-piperidinyl)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-, (4aS,8aR)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-49-0 CAPLUS
CN 1(2H)-Phthalezinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-[{2-cxo-2H-1-benzopyran-7-y1]methyl}-4-piperidinyl]-, (4aS,8aR)- (9CI) (CA INDEX NAME)

L4 ANSWER 3 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

449760-50-3 CAPLUS

CN Morpholine,
4-[(4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro1-oxo-2(1H)-phthalazinyl)-1-piperidinyl]acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-51-4 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(2-phenylethyl)-4-piperidinyl]-, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 3 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

449760-56-9 CAPLUS 1(2H)-Phthalazinone, 3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-[[4-(1,2,3-thiadiazol-4-yl)phenyl]methyl]-4-piperidinyl]-, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

449760-57-0 CAPLUS
Benzoic acid, 4-{{[4-{4as,8aR}-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl}-1-piperidinyl|acetyl]amino}-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 3 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

449760-52-5 CAPLUS
1(2H)-Phthalazinone,
,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(3pyridinylmethyl)-4-piperidinyl}-, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-53-6 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-{2-pyridinylmethyl}-4-piperidinyl]-, {4aS,8aR}- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 3 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

449760-58-1 CAPLUS
1-Piperidineacetamide, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl)- (9CI) (CA INDEX NAME)

RN 596102-01-1 CAPLUS CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-{1-(1-methylethyl)-4-piperidinyl]- (9CI) (CA INDEX NAME)

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L4 ANSWER 3 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

596102-07-7 CAPLUS

CN Piperidine,
4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-(4-morpholinylacetyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 596102-09-9 CAPLUS
CN Piperidine,
4-[(4as, 8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo2(1H)-phthalazinyl]-1-[(4-{2-(dimethylamino)ethyl}-1-piperazinyl]acetyl](9CI) (CA INDEX NAME)

Absolute stereochemistry

L4 ANSWER 4 OF 22 CAPLUS COPYRIGHT 2007 ACS ON STN ACCESSION NUMBER: 2004:1036929 CAPLUS CAPLUS 142:16825

DOCUMENT NUMBER: TITLE:

INVENTOR(S):

142:16825 Composition comprising a PDE4 inhibitor and a PDE5 inhibitor Dunkern, Thoraten; Hatzelmann, Armin; Schudt, Christian; Grimminger, Friedrich; Ghofrani, Hossein

Christian; Grimminger, Friedi Ardeschir Altana Pharma A.-G., Germany PCT Int. Appl., 43 pp. CODEN: PIXXD2 Patent

PATENT ASSIGNEE(S): SOURCE:

DOCUMENT TYPE: LANGUAGE: English

FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE PATENT NO. KIND DATE APPLICATION NO. DATE

NO 2004103407*

**N: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BM, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MM, MX, MZ, NA, NI, NI, NO, NZ, OM, PG, PH, PL, FT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BM, GH, GM, KE, LS, MM, MZ, MA, NI, AT, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IB, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BP, BJ, CP, CG, CI, CM, GM, GM, GM, MK, MN, MK, MK, MK, AR, NE, SN, TD, TG

AU 2004241749

AU 2004251946**

AU 20041202**

AU 2004-2525946**

AU 20041203**

AU 2004-2525946**

AU 20041201**

AU 2004-2525946**

AU 2004-519**

BE, AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LLI, LU, NL, SE, MC, PT, SE, MC, P 20041202 SN, TD, TG
[241749 Al 20041202 AU 2004-241749 20040519
[3946 Al 20041202 CA 2004-2525946 20040519
[662] A2 20060301 EP 2004-766017
AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
1E, SI, LT, LV, PI, RO, MK, CY, AL, TR, BG, C2, EE, HU, PL, SK, 20060523 20060621 20061214 20060504 20051214 WO 2004-EP50869

ANSWER 3 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

REFERENCE COUNT:

THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

ANSWER 4 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

AB The invention relates to the combined administration of a PDE4 inhibitor and a PDE5 inhibitor for the treatment of a disease in which phosphodiesterase 4 (PDE4) and/or phosphodiesterase 5 (PDE5) activity is detrimental. Patients were administered orally one tablet of Roflumilase and once daily a tablet of Viagra. An example of another selected PDE4 inhibitor is 1.

IT 449760-14-9 449760-15-0 449760-16-1
449760-17-2 449760-19-4 449760-20-7
449760-21-8 449760-22-9 449760-21-0 449760-31-0 4497

L4 ANSWER 4 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 449760-15-0 CAPLUS CN Piperidine, 4-[(445,848)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-(methylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

449760-16-1 CAPLUS
Piperidine, 1-acetyl-4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

ANSWER 4 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

449760-20-7 CAPLUS 1-Piperidinecarboxamide, 4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-phenyl-(9CI) (CA INDEX RAME)

Absolute stereochemistry.

449760-21-8 CAPLUS
1-Piperidinecarboxamide, 4-{(4a5,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl}-N-(1,1-dimethylethyl}- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 4 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 449760-17-2 CAPLUS
CN 1-Piperidinepentanoic acid,
4-[(4aS,8aR]-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-5-oxo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

449760-19-4 CAPLUS
1-Piperidinecarboxamide, 4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-ox-2(1H)-phthalazinyl)-N-(1,1-dimethylethyl)- (9CI) (CA

Absolute stereochemistry.

L4 ANSWER 4 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

449760-22-9 CAPLUS 1-Piperidinecarboxamide, 4-[(4aR,8aS)-4-(2,3-dihydro-7-methoxy-2,2-

dimethyl-4-benzofuranyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N(1,1-dimethylethyl)-, rel- (9CI) (CA INDEX NAME)

449760-23-0 CAPLUS
Piperidine, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl)-1-[[5-(dimethylamino)-1-naphthalenyl]sulfonyl}-(9CI) (CA INDEX NAME)

L4 ANSWER 4 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

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PAGE 2-A

RN 449760-24-1 CAPLUS CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(4nitrophenyl)-4-piperidinyl]-, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 4 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 449760-27-4 CAPLUS
CN 1(2R)-Phthalazinone, 2-[1-[2-(4-amino-3,5-dichloropheny1)-2-oxoethyl]-4piperidinyl]-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-,
monohydrochloride, (4eS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry

RN 449760-28-5 CAPLUS
CN 1(2H)-Phthalazinone,
(-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-{1-{1methyl-1H-pyrazolo(3,4-d)pyrimidin-4-yl)-4-piperidinyl}- (9CI) (CA INDEX NAME)

L4 ANSWER 4 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 449760-25-2 CAPLUS CN 1(2H)-Phthalazinone, 4-(3.4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(4pyridinylmethyl)-4-piperidinyl]-, (4a5,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-26-3 CAPLUS CN Morpholine, 4-[[4-[(468,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 4 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

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PAGE 1-A

RN 449760-29-6 CAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-(1-thieno(2,3-d)pyrimidin-4-yl-4-piperidinyl)-, (4aS,8aR)- (9CI) (CA INDEX NAME)

L4 ANSWER 4 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

(Continued)

PAGE 1-A

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RN 449760-30-9 CAPLUS CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-(1-(2-pyrimidinyl)-4-piperidinyl]-, (4a5,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

ANSWER 4 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued) Oxo-2(1H)-phthalazinyl]-1-piperidinyl]carbonyl]- (CA INDEX NAME)

Absolute stereochemistry.

449760-40-1 CAPLUS
1-Piperidineacetamide, 4-[{4aS,8aR}-4-(3,4-dimethoxyphenyl}-4a,5,8,8a-terrahydro-1-oxo-2(1H)-phthalazinyl}-N-(1-methylethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

449760-42-3 CAPLUS
2,3-Piperaxinedione, 1-[[4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]carbonyl]-4-ethyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 4 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 449760-31-0 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-48,5,8,8a-tetrahydro-2-[1-[(2-oxo-2H-1-benzopyran-7-yl)methyl]-4-piperidinyl]-, monohydrochloride,
(4eS,8aR)- (9Cl) (CA INDEX NAME)

Absolute stereochemistry.

● HC1

RN 449760-35-4 CAPLUS CN Morpholine, 4-[[4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-

ANSWER 4 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

449760-47-8 CAPLUS
Piperidine,
-{{4as,8aB,-4-{1,4-diethoxyphenyl}-4a,5,8,8a-tetrahydro-1-oxo-2(1H}-phthalazinyl]-1-{4-pyridinylcarbonyl}- (9CI) {CA INDEX NAME}

CN Morpholine,
4-[[4-[[4-8],8aR]-4-(3,4-dimethoxyphenyl]-4a,5,8,8a-tetrahydro1-0xo-2(1H)-phthalazinyl]-1-piperidinyl]acetyl]- (9Cl) (CA INDEX NAME)-

L4 ANSWER 4 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 449760-51-4 CAPLUS CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4e,5,8,8a-tetrahydro-2-(1-{2-phenylethyl)-4-piperidinyl]-, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-52-5 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(3-pyridinylmethyl)-4-piperidinyl]-, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

ANSWER 4 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 449760-55-8 CAPLUS
CN 1-Piperazineethanamine,
4-[(48,8a8)-4-(3,4-diethoxyphenyl)-4a,5,8,8atetrahydro-1-0xo-2(1H)-phthalazinyl]-1-piperidinyl]acetyl]-N,N-dimethyl(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-56-9 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-[4[1,2,3-thiadiazol-4-yl)phenyl]methyl]-4-piperidinyl]-, (4aS,8aR)- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 4 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 449760-53-6 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-{1-(2pyridinylmethyl)-4-piperidinyl]-, (4aS,8aR}- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-54-7 CAPLUS
CN Morpholine,
4-[[4-[(48,8aR)+4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]acetyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

ANSWER 4 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

449760-57-0 CAPLUS
Benzoic acid, 4-{[(4-{(4as,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]acetyl]amino]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

449760-58-1 CAPLUS
1-Piperidineacetamide, 4-[(4a5.8aR)-4-(3.4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]- (9CI) (CA INDEX NAME)

ANSWER 4 OF 22 CAPLUS COPYRIGHT 2007 ACS OR STN (Continued)

ANSWER 5 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

449760-15-0 CAPLUS
Piperidine,
([4as,8a8]-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo2(1H)-phthalazinyl]-1-(methylsulfonyl)- (9CI) (CA INDEX NAME)

449760-16-1 CAPLUS
Piperidine, 1-acetyl-4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl)- (9CI) (CA INDEX NAME)

FAMILY ACC. NUM. COUNT: PATENT INFORMATION: MO 2004098633 A1 20041118 MO 2004-EP50748 20040510
M: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BM, BY, BZ, CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EB, EG, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KB, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MM, MX, MZ, NA, NI,
NO, NZ, OM, PQ, FH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SY,
TJ, TM, TN, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RN: BW, GH, GM, KE, LS, MM, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, FT, RO, SE,
SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
PRIORITY APPLN: INFO: ABOUTT APPLN. INFO.: EP 2003-10581 A 20030512

AB The invention relates to the combined administration of a PDE4 inhibitor and a TMF0 antagoniet selected from the group consisting of etanercept, onercept and pegaunercept for the treatment of a disease in which phosphodiesterase 4 (PDE4) and/or tumor necrosis factor alpha (TMF0) activity is decrimental.

IT 449760-14-9 449760-15-0 449760-16-1
449760-14-9 449760-15-0 449760-16-1
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449760-21-8 449760-22-9 449760-23-0
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449760-50-1 449760-51-6 449760-51-6
449760-50-1 449760-51-7 449760-51-8
449760-15-6 449760-51-7 449760-51-8
(Biological study); USE5 (Uses)
(Cherapeutic activity of phosphodiesterase 4 inhibitors and TNF0 antagonists)
RN 449760-14-9 CAPLUS
RN 449760-14-9 CAPLUS
CN Piperidine,
4-(14-405-80R)-4-(14-4-diethoxyphenyl)-4a-5,8,8a-tetrahydro-1-oxo-21H1-phthalazinyl]-1-((4-methylphenyl)sulfonyl)- (9CI) (CA INDEX NAME)

ANSWER 5 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

Absolute stereochemistry.

449760-17-2 CAPLUS 1-Piperidinepentanoic acid, (48,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-5-oxo- (9CI) (CA INDEX NAME)

449760-19-4 CAPLUS
1-Piperidinecarboxamide, 4-{{4aS,8aR}-4-(3,4-diethoxyphenyl}-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)

L4 ANSWER 5 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

449760-20-7 CAPLUS
1-Piperidinecarboxamide, 4-{{4aS,8aR}-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl}-N-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

449760-21-8 CAPLUS
1-Piperidinecarboxamide, 4-[{4aS,8aR}-4-{3,4-dimethoxyphenyl}-4a,5,8,8a-tetrshydro-1-oxo-2(1H)-phthalazinyl]-N-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

ANSWER 5 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

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RN 449760-24-1 CAPLUS
CN 1(2H)-Phthalazinone.
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-{4-nitrophenyl}-4-piperidinyl}-, (4eS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 5 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

449760-22-9 CAPLUS 1-Piperidinecarboxamide, 4-[(4aR,8aS)-4-(2,3-dihydro-7-methoxy-2,2-

 $\label{lem:dimethyl-4-benzofuranyl} \mbox{-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl} \mbox{-NAME} \\ \mbox{(1,1-dimethylethyl)-, rel- (9CI) (CA INDEX NAME)}$

Relative stereochemistry.

449760-23-0 CAPLUS
Piperidine, 4-[(4aS,8aR]-4-(3,4-dimethoxyphenyl)-4a.5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-[[5-(dimethylamino)-1-naphthalenyl]sulfonyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

ANSWER 5 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 449760-25-2 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-(1-(4-pyridinylmethyl)-4-piperidinyl]-, (4aS,8aR)- (9Cl) (CA INDEX NAME)

RN 449760-26-3 CAPLUS
CN Morpholine,
4-[[4-[468,58R]-4-[3,4-dimethoxyphenyl]-4e,5,8,8a-tetrahydro1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]carbonyl]- (9CI) (CA INDEX NAME)

L4 ANSWER 5 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 449760-28-5 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3, 4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(1methyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)-4-piperidinyl]- (9CI) (CA INDEX NAME)

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L4 ANSMER 5 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(2-pyrimidinyl)-4-piperidinyl]-, (4a3,8aR)- (9CI) (CA INDEX NAME) (Continued)

Absolute stereochemistry.

RN 449760-35-4 CAPLUS
CN Morpholine,
4-[[4-[(48,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1oxo-2(1H)-phthalazinyl}-1-piperidinyl]carbonyl]- (9CI) (CA INDEX NAME)

449760-40-1 CAPLUS
1-Piperidineacetamide, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalaxinyl]-N-(1-methylethyl)- [9CI] (CA INDEX NAME)

L4 ANSWER 5 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

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449760-29-6 CAPLUS
1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-(1-thieno[2,3-d]pyrimidin-4-yl-4-piperidinyl)-, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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449760-30-9 CAPLUS

L4 ANSWER 5 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN Absolute stereochemistry. (Continued)

449760-42-3 CAPLUS 2,3-Piperazinedione, 1-[[4-{(4aS,8aR}-4-{3,4-dimethoxyphenyl}-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl}-1-piperidinyl}carbonyl}-4-ethyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN' 449760-47-8 CAPLUS CN Piperidine, 4-{(448,588)-4-{3,4-diethoxyphenyl}-48,5,8,88-tetrahydro-1-oxo-2(1H)-phthalazinyl}-1-(4-pyridinylcarbonyl)- (9CI) (CA INDEX NAME)

L4 ANSWER 5 OF 22 CAPLUS COPYRIGHT 2007 ACS ON STN (Continued)

449760-48-9 CAPLUS
1(2H)-Phthalazinone, 2-[1-[2-(4-amino-3,5-dichlorophenyl)-2-oxoethyl]-4-piperidinyl]-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-, (4aS,8aR)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-49-0 CAPLUS CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-[(2-oxo-2H-1-benzopyran-7-yl)methyl]-4-piperidinyl]-, (4as,8aR)- (9CI) (CA

L4 ANSWER 5 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN Absolute stereochemistry. (Continued)

RN 449760-52-5 CAPLUS CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(3-pyridinylmethyl)-4-piperidinyl]-, (4aS,8aR)-, (9CI) (CA INDEX NAME)

RN 449760-53-6 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(2pyridinylmethyl)-4-piperidinyl]-, (4a5,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

ANSWER S OF 22 CAPLUS COPYRIGHT 2007 ACS ON STN INDEX NAME) (Continued)

Absolute stereochemistry.

449760-50-3 CAPLUS

CN Morpholine,
4-[[4-[(445,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro1-oxo-2(lH)-phthalazinyl]-1-piperidinyl]acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-51-4 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(2-phenylethyl)-4-piperidinyl]-, (4aS,8aR)- (9CI) (CA INDEX NAME)

ANSWER 5 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 449760-54-7 CAPLUS '
CN Morpholine,
4-[[4-[448,8eR]-4-[3,4-diethoxyphenyl]-4e,5,8,8e-tetrahydro-1oxo-2(1H)-phthalazinyl]-1-piperidinyl]acetyl]- (9CI) (CA INDEX NAME)

RN 449760-55-8 CAPLUS
CN 1-Piperazineethanamine,
4-[(485.8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8atetrahydro-1-0xo-2(1H)-phthalazinyl]-1-piperidinyl]acetyl]-N,N-dimethyl(9CI) (CA INDEX NAME)

ANSWER 5 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 449760-56-9 CAPLUS
CN 1(3H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-[(4-(1,2,3-thiadiazol-4-yl)phenyl]methyl]-4-piperidinyl]-, (4a5,8aR)- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

449760-57-0 CAPLUS
Benzoic acid, 4-[[{4-[{4as,8aR}-4-(3,4-dimethoxyphenyl}-4a,5,8,8a-tetrahydro-1-oxo-2(lR)-phthalazinyl}-1-piperidinyl]acetyl]amino]-, ethyl ester (9C1) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 6 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:
DOCUMENT NUMBER:
141:406664
Composition comprising a PDE4 inhibitor and soluble human Type II interleukin-1 receptor (shuIL-1RII) for disease therapy
BATENT ASSIGNEE(S):
SOURCE:
DOCUMENT TYPE:
LANGUAGE:
PAMILY ACC. NUM. COUNT:
LANGUAGE:
PAMILY ACC. NUM. COUNT:
PATENT INPORMATION:

DOCUMENT TYPE: LANGUAGE: PAMILY ACC. NUM. COUNT: PATENT INFORMATION:

PATENT NO.	KIND DATE .	APPLICATION NO.	DATE				
			20040510				
WO 2004098606	A1 20041118	WO 2004-EP50749					
W: AE, AG, AL,	AM, AT, AU, AZ,	BA, BB, BG, BR, BW, BY,	BZ, CA, CH,				
CN, CO, CR,	CU, CZ, DE, DK,	DM, DZ, EC, EE, EG, ES,	FI, GB, GD,				
GE, GH, GM,	HR, HU, ID, IL,	IN, IS, JP, KE, KG, KP,	KR, KZ, LC,				
LK, LR, LS,	LT, LU, LV, MA,	MD, MG, MK, MN, MW, MX,	MZ, NA, NI,				
NO, NZ, OM,	PG, PH, PL, PT,	RO, RU, SC, SD, SE, SG,	SK, SL, SY,				
TJ, TM, TN,	TR, TT, TZ, UA,	UG, US, UZ, VC, VN, YU,	ZA, ZM, ZW				
RW: BW, GH, GM,	KE, LS, MW, MZ,	NA, SD, SL, SZ, TZ, UG,	ZM, ZW, AM,				
AZ, BY, KG,	KZ, MD, RU, TJ,	TM, AT, BE, BG, CH, CY.	CZ, DE, DK,				
EE, ES, PI,	FR, GB, GR, HU,	IE, IT, LU, MC, NL, PL,	PT, RO, SE,				
SI, SK, TR,	BF, BJ, CF, CG,	CI, CM, GA, GN, GQ, GW,	ML, MR, NE,				
SN, TD, TG							
PRIORITY APPLN. INFO.:		EP 2003-10596 A	20030512				

The invention relates to the combined administration of a PDE4 inhibitor and shull-1R II for the treatment of a disease in which phosphodiesterase 4 (PDE4) and/or interleukin-1 (IL-1) activity is detrimental. 449760-18-1 449760-15-0 449760-16-1 449760-17-2 449760-19-4 449760-16-1 449760-17-2 449760-22-9 449760-22-0 449760-23-0 449760-24-1 449760-22-9 449760-23-0 449760-24-1 449760-25-2 449760-26-9 449760-30-9 449760-31-4 449760-31-6 4

RN 449760-14-9 CAPLUS
CN Piperidine,
4-[(445,848]-4-(3,4-diethoxyphenyl)-48,5,8,8a-tetrahydro-1-oxo2(1H)-phthalazinyl)-1-[(4-methylphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

ANSWER 5 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

449760-58-1 CAPLUS Piperidineacetamide, 4-{(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalarinyl}- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

REFERENCE COUNT:

THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

ANSWER 6 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 449760-15-0 CAPLUS CN Piperidine, 4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl)-1-(methylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

449760-16-1 CAPLUS
Piperidine, 1-acetyl-4-[(4as,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl)- (9CI) (CA INDEX RAME)

L4 ANSWER 6 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 449760-17-2 CAPLUS
CN 1-Piperidinepentanoic acid,
4-[(4aS.88R)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-8-oxo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-19-4 CAPLUS
CN 1-Piperidinecarboxamide, 4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl}-N-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 6 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 449760-22-9 CAPLUS
CN 1-Piperidinecarboxamide, 4-[(4aR,8aS)-4-(2,3-dihydro-7-methoxy-2,2-

dimethyl-4-benzofuranyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl}-N(1,1-dimethylethyl)-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

RN 449760-23-0 CAPLUS
CN Piperidine, 4-[(4aS, BaR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1oxo-2(1H)-phthalazinyl)-1-[[5-(dimethylamino)-1-naphthalenyl)sulfonyl}(9C1) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 6 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 449760-20-7 CAPLUS
CN 1-Piperidinecarboxamide, 4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-phenyl- (9Cl) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-21-8 CAPLUS
CN 1-Piperidinecarboxamide, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl)-N-(1,1-dimethylethyl)- (9CI) (CA INDEX RAME)

Absolute stereochemistry

L4 ANSWER 6 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

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RN 449760-24-1 CAPLUS CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4e,5,8,8a-tetrahydro-2-[1-(4nitrophenyl)-4-piperidinyl]-, (4aS,8aR)- (9CI) (CA INDEX NAME)

ANSWER 6 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 449760-25-2 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(4pyridinylmethyl)-4-piperidinyl]-, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-26-3 CAPLUS
CN Morpholine,
4-[[4-[[4-2](485,88R)-4-(3,4-dimethoxyphenyl)-4e,5,8,8a-tetrahydro1-0x0-2(1H)-phthalazinyl]-1-piperidinyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 6 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

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449760-29-6 CAPLUS
1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-(1-thieno[2,3-d]pyrimidin-4-yl-4-piperidinyl)-, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

(Continued)

PAGE 2-A

RN 449760-30-9 CAPLUS
CN 1(2H)-Phthalazinone.
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-{2-pyrimidinyl}-4-piperidinyl}-, (4eS,8aR)- (9CI) (CA INDEX NAME)

L4 ANSWER 6 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 449760-28-5 CAPLUS
CN 1(2H)-Phthalazinone,
-(3, 4-dimethoxyphenyl)-4a,5,8.8a-tetrahydro-2-(1-(1-methyl-1H-pyrazolo(3,4-d)pyrimidin-4-yl)-4-piperidinyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

L4 ANSWER 6 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN Absolute stereochemistry. (Continued)

RN 449760-35-4 CAPLUS
CN Morpholine,
4-[[4-([4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1oxo-2(lH)-phthalazinyl)-1-piperidinyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

449760-40-1 CAPLUS
1-Piperidineacetamide, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-(1-methylethyl)- (9CI) (CA INDEX NAME)

L4 ANSWER 6 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

449760-42-3 CAPLUS 2,3-Piperazinedione, 1-[[4-[{4aS,8aR}-4-(3,4-dimethoxyphenyl]-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl}-1-piperidinyl]carbonyl]-4-ethyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-47-8 CAPLUS
CN Piperidine,
4-[(4a8,8aR)-4-(1,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-(4-pyridinylcarbonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

ANSWER 6 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN INDEX NAME) (Continued)

Absolute stereochemistry.

449760-50-3 CAPLUS

CN Morpholine, 4-[[4-[[4s,58R]-4-(3,4-dimethoxyphenyl]-4s,5,8,8a-tetrahydro-l-oxo-2[HH-phthalazinyl]-1-piperidinyl]scetyl]- [SCI] (CA INDEX NAME)

RN 449760-51-4 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-(1-(2-phenylethyl)-4-piperidinyl)-, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 6 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

449760-48-9 CAPLUS 1(2H)-Phthalazinone, 2-(1-{2-(4-amino-3,5-dichlorophenyl)-2-oxoethyl}-4-piperidnyl)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-, (4aS,8aR)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-49-0 CAPLUS CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-[(2-oxo-2H-1-benzopyran-7-yl)methyl]-4-piperidinyl]-, (4as,8aR)- (9CI) (CA

L4 ANSWER 6 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 449760-52-5 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(3-pyridinylmethyl)-4-piperidinyl}-, (4aS,8aR)- (9CI) (CA INDEX NAME)

RN 449760-53-6 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-{1-{2pyridinylmethyl}-4-piperidinyl}-, (4aS,8aR)- (9CI) (CA INDEX NAME)

L4 ANSWER 6 OF 22 CAPLUS COPYRIGHT 2007 ACS ON STN (Continued)

RN 449760-54-7 CAPLUS CN Morpholine, 4-{[4-[(48,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]acetyl}- (9CI) (CA INDEX NAME)

RN 449760-55-8 CAPLUS
CN 1-Piperazineethanamine,
4-[(4-(485,8a8)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-0xo-2(1H)-phthalazinyl]-1-piperidinyl]acetyl}-N,N-dimethyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

ANSWER 6 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

449760-58-1 CAPLUS
1-Piperidineactamide, 4-[(4a5,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl)- (9Cl) (CA INDEX NAME)

Absolute stereochemistry.

REPERENCE COUNT

FORMAT

THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

L4 ANSWER 6 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

RN 449760-56-9 CAPLUS CN 1(3H)-Phthalazinone, 4-(3,4-dimethoxypheny))-4a,5,8,8a-tetrahydro-2-[1-[[4-(1,2,3-thiadiazol-4-yl)phenyl]methyl]-4-piperidinyl]-, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

449760-57-0 CAPLUS
Benzoic acid, 4-{[{4-[{4a5,8aR}-4-(3,4-dimethoxyphenyl}-4a,5,8,8a-tetrahydro-1-oxo-2(HB-phthalazinyl}-1-piperidinyl]acetyl]amino]-, ethylester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 7 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:995978 CAPLUS
DOCUMENT NUMBER: 141:460663
TITLE: Pharmaceutical composition comprising a PDE4 . inhibitor

and IL-1 trap for treatment of disease Barsig, Johannes Altane Pharma AG, Germany PCT Int. Appl., 24 pp. CODEN: PIXXD2 Patent Int. Appl., 25 pp. INVENTOR (5):

PATENT ASSIGNEE(S): SOURCE:

DOCUMENT TYPE: LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

PATENT NO.					KIND DATE				APPLICATION NO.						DATE				
WO 2004098605				A1 20041118			1	WO 2	004-	EP50	20040510								
	W:	ΑE,	AG,	AL,	AM,	AT,	AU,	AZ,	BA,	BB,	BG,	BR,	BW,	BY,	BZ,	CA,	CH,		
		CN,	co,	CR,	Cυ.	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	EG,	ES,	PI,	GB,	GD,		
		GE,	GH,	GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	KP,	KR.	KZ.	LC.		
		LK,	LR,	LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ.	NA.	NI.		
		NO,	NZ,	OM,	PG,	PH,	PL,	PT,	RO,	RU,	SC,	SD,	SE.	SG.	SK.	SL.	SY.		
		TJ,	TM,	TN,	TR,	TT,	TZ,	UA,	UG,	US,	UZ,	VC,	VN,	YU,	ZA,	ZM,	ZW		
	RW:	BW,	GH,	GM,	KE,	LS,	MW,	MZ,	NA.	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,		
		AZ,	BY,	KG,	KZ.	MD,	RU,	TJ,	TM,	AT,	BE,	BG,	CH,	CY,	CZ,	DE.	DK.		
		EE,	ES,	PI,	FR.	GΒ,	GR,	HU,	IE.	IT,	LU,	MC.	NL,	PL.	PT.	RO.	SE.		
			SK,																
			TD,																
ORITY	APP	LN.	inpo	. :						EP 2	003-	1063	1		1 2	0030	512		

The invention relates to the combined administration of a PDE4 inhibitor and IL-1 Trap for the treatment of a disease in which phosphodiesterase 4 (PDE4) and/or interleukin-1 (IL-1) activity is detrimental. 449760-14-9 449760-15-0 449760-16-1 449760-17-2 449760-19-4 449760-18-1 449760-17-2 449760-19-4 449760-20-7 449760-18-4 449760-22-9 449760-23-0 449760-18-5 449760-18-5 449760-18-6 49760-18-

for treatment of disease)

RN 449760-14-9 CAPLUS

CN Piperidine,
-[(445,848)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl)-1-[(4-methylphenyl)sulfonyl)- (9CI) (CA INDEX NAME)

ANSWER 7 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

RN 449760-15-0 CAPLUS CN Piperidine, 4-[(485,887)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalezinyl]-1-(methylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

449760-16-1 CAPLUS
Piperidine, 1-acetyl-4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 7 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

449760-20-7 CAPLUS
1-Piperidinecarboxamide, 4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl)-N-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

449760-21-8 CAPIUS
1-Piperidinecarboxamide, 4-{{4aS,8aR}-4-{3,4-dimethoxyphenyl}-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalexinyl}-N-{1,1-dimethylethyl}- (9CI) (CA INDEX RAME)

Absolute stereochemistry.

L4 ANSWER 7 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

RN 449760-17-2 CAPLUS
CN 1-Piperidinepentanoic acid,
4-{(4a5,8a7)-4-(3,4-diethoxyphenyl)-4a,5,8,8atetrahydro-1-oxo-2(1H)-phthalazinyl]-8-oxo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

449760-19-4 CAPLUS
1-Piperidinecarboxamide, 4-[(4aS,8aR)-4-(3,4-diethoxyphanyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl)-N-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 7 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

449760-22-9 CAPLUS 1-Piperidinecarboxamide, 4-[(4aR,8aS)-4-(2,3-dihydro-7-methoxy-2,2-

dimethyl-4-benzofuranyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N(1,1-dimethylethyl)-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

449760-23-0 CAPLUS
Piperidine, 4-[(485,88R)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1cxo-2(1H)-phthalazinyl]-1-{{5-(dimethylamino)-1-naphthalenyl]sulfonyl](9C1) (CA INDEX RAME)

L4 ANSWER 7 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

Meo NMe 2

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RN 449760-24-1 CAPLUS CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(4nitrophenyl)-4-piperidinyl]-, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 7 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 449760-28-5 CAPLUS
CN 1(2H)-Phthalazinone,
4:(3,4-dimethoxyphenyl)-4s,5,8,8s-tetrahydro-2-[1-(1methyl-1H-pyrazolo(3,4-d]pyrimidin-4-yl)-4-piperidinyl]- (9CI) (CA INDEX NAME)

L4 ANSWER 7 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 449760-25-2 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3.4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(4pyridinylmethyl)-4-piperidinyl]-, (4a5,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-26-3 CAPLUS
CN Morpholine,
4-[[4-[(4aS,8aR)-4-[3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro1-0x0-2(1H)-phthalazinyl]-1-piperidinyl]carbonyl]- (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 7 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

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RN 449760-29-6 CAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-(1-thieno[2,3-d]pyrimidin-4-yl-4-piperidinyl)-, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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RN 449760-30-9 CAPLUS
CN 1(2H)-Phthalarinome,
4-(3,4-dimethoxyphenyl)-4-a,5,8,8a-tetrahydro-2-[1-(2pyrimidinyl)-4-piperidinyl]-, (4a5,8aR)- (9CI) (CA INDEX NAME)

L4 ANSWER 7 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 449760-35-4 CAPLUS
CN Morpholine,
4-[{4-[{48,8aR}}-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1cxo-2(1H)-phthalazinyl]-1-piperidinyl|carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

449760-40-1 CAPLUS
1-Piperidineacetamide, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-(1-methylethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

ANSWER 7 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

449760-48-9 CAPLUS 1(2H)-Phthalazinone, 2-[1-{2-(4-amino-3,5-dichlorophenyl)-2-oxoethyl}-4-piperidinyl]-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-, (4eS,8aR)-(9CI) (CA INDEX NAME)

RN 449760-49-0 CAPLUS
CN 1(2H)-Phthalaxinone,
4-(3.4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-[(2-oxo-2H-1-benzopyran-7-yl]methyl]-4-piperidinyl]-, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 7 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

449760-42-3 CAPLUS
2.3-Piperazinedione, 1-[{4-{(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl)carbonyl}-4-ethyl-(9C1) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-47-8 CAPLUS
CN Piperidine,
4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-(4-pyridinylcarbonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 7 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

RN 449760-50-3 CAPLUS
CN Morpholine,
4-{[4-[(48,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro1-oxo-2(1H)-phthalazinyl]-1-piperidinyllacetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-51-4 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(2-phenylethyl)-4-piperidinyl]-, (4eS,8aR)- (9CI) (CA INDEX NAME)

L4 ANSWER 7 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 449760-52-5 CAPLUS CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(3-pyridinylmethyl)-4-piperidinyl]-, (4eS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-53-6 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(2-pyridinylmethyl)-4-piperidinyl]-, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

ANSWER 7 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

449760-56-9 CAPLUS
1(2H)-Phthalarinone,
3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-{1-{{4-}
(1,2,3-thiadiazol-4-yl)phenyl]methyl}-4-piperidinyl}-, (4aS,8aR)- (9CI)
(CA INDEX NAME)

449760-57-0 CAPLUS
Benzoic acid, 4-{[[4-[(4s,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1R)-phthalazinyl]-1-piperidinyl]acetyl]amino]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 7 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 449760-54-7 CAPLUS CN Morpholine, 4-{[4-{(48,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-55-8 CAPLUS
CN 1-Piperazineethanamine,
4-[(4-(4s5,8a8)-4-(3,4-diethoxyphenyl)-4a,5,8,8atetrahydro-1-0xo-2(1H)-phthalazinyl]-1-piperidinyl]acetyl]-N,N-dimethyl(9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 7 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

449760.58-1 CAPLUS
1-Piperidineactamide, 4-[(485,88R)-4-(3,4-dimethoxyphenyl)-4e,5,8,8a-terrahydro-1-oxo-2(1H)-phthalazinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

REFERENCE COUNT:

THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L4 ANSMER 8 OF 22
ACCESSION NUMBER:
DOCUMENT NUMBER:
11:41602
Composition comprising a PDE4 inhibitor and a TNFW antagonist
Barrig, Johannes; Weimar, Christian
Altana Pharma AG, Germany
PCT Int. Appl. . 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

PATENT NO. DATE APPLICATION NO. DATE KIND WO 2004098578 WO 2004098578 WO 2004098578

W: AE, AG, AI
CN, CO, CR
GE, GH, CW
LK, LR, LS
NO, N2, OW
TJ, TM, TM
RN: SN, GH, GW
AZ, BY, KG
EE, ES, FI
SN, TD, TO
PRIORITY APPLN: INFO:: EP 2003-10593

The invention relates to the combined administration of a PDE4 inhibitor and a TNPx antagonist selected from the group consisting of infliximab, adalimumab, cdp870 and cdp571 for the treatment of a disease in which phosphodiesterase 4 (PDE4) and/or tumor necrosis factor alpha (TNPx) activity is detrimental.
449760-14-9 449760-15-0 449760-16-1
449760-17-2 449760-15-0 449760-20-7
449760-21-2 449760-22-9 449760-22-0
449760-24-1 449760-25-2 449760-26-3
449760-24-1 449760-25-2 449760-30-9
449760-35-4 449760-40-1 449760-42-3
449760-50-3 449760-51-4 449760-52-5
449760-50-6 449760-51-4 449760-55-5
449760-50-6 449760-51-7 049760-55-8
419760-50-6 9449760-51-7 049760-58-1
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (pharmaceutical injections containing phosphodiesterase 4 inhibitors

combination with TNFu antagonists for treatment of arthritis and other diseases)
449760-14-9 CAPLUS
Piperidine,
(448.88R)-4-(3.4-diethoxyphenyl)-4a,5.8,8a-tetrahydro-1-oxo2(1H)-phthalszinyl]-1-{(4-methylphenyl)sulfonyl}- (9CI) (CA INDEX NAME)

(Continued)

ANSWER 8 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

449760-17-2 CAPLUS
1-Piperidinepentanoic acid,
[485,887]-4-(3,4-diethoxyphenyl)-48,5,8,8atetrahydro-1-oxo-2(1H)-phthalazinyl]-8-oxo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

449760-19-4 CAPLUS
1-Piperidinecarboxamide, 4-{{4aS,8aR}-4-{3,4-diethoxyphenyl}-4a,5,8,8a-tetrahydro-1-oxo-2{lH}-phthalazinyl}-N-{1,1-dimethylethyl}- (9CI) (CA-INDEX_MAME)

L4 ANSWER 8 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN Absolute stereochemistry. (Continued)

RN 449760-15-0 CAPLUS
CN Piperidine,
4-[(445,884)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo2(1H)-phthalazinyl]-1-(methylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

449760-16-1 CAPLUS
Piperidine, 1-acetyl-4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl)- (9CI) (CA INDEX NAME)

ANSWER 8 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

449760-20-7 CAPLUS 1-Piperidinecarboxamide, 4-{(4a5,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-phenyl- (9CI) (CA INDEX NAME)

449760-21-8 CAPLUS
1-Piperidinecarboxamide, 4-{(4aS,8aR)-4-{3,4-dimethoxyphenyl}-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl}-N-{1,1-dimethylethyl}- {9CI} (CA INDEX NAME)

L4 ANSWER 8 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

449760-22-9 CAPLUS
1-Piperidinecarboxamide, 4-[(4aR,8aS)-4-(2,3-dihydro-7-methoxy-2,2-

dimethyl-4-benzofuranyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl)-N(1,1-dimethylethyl)-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

449760-23-0 CAPLUS
Piperidine, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-[[5-(dimethylamino)-1-naphthalenyl]sulfonyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

ANSWER 8 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 449760-25-2 CAPLUS CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(4-pyridinylmethyl)-4-piperidinyl]-, (4as,8aR)- (9CI) (CA INDEX NAME)

RN 449760-26-3 CAPLUS
CN Morpholine,
4-[[4-[483,88R]-4-[3,4-dimethoxyphenyl]-4e,5,8,8a-tetrahydro1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]carbonyl]- (9Cl) (CA INDEX NAME)

L4 ANSWER 8 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

PAGE 1-A

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RN 449760-24-1 CAPLUS CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-{4-nitrophenyl)-4-piperidinyl]-, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 8 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

449760-28-5 CAPLUS
1(2H)-Phthalazinone,
4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(1-methyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)-4-piperidinyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

L4 ANSWER 8 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

PAGE 2-A

449760-29-6 CAPLUS
1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-(1-thieno(2,3-d]pyrimidin-4-yl-4-piperidinyl)-, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

RN 449760-30-9 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-{1-(2-

ANSWER 8 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN NAME) (Continued)

449760-42-3 CAPLUS
2,3-Piperazinedione, 1-[[4-[{4aS,8aR}]-4-{3,4-dimethoxyphenyl}-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]carbonyl]-4-ethyl-(SCI) (CA INDEX RAME)

Absolute stereochemistry.

RN 449760-47-8 CAPLUS
CN Piperidine,
4-[(445,881)-4-(3,4-diethoxyphenyl)-48,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl)-1-(4-pyridinylcarbonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

ANSMER 8 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued) pyrimidinyl}-4-piperidinyl}-, (4as,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-35-4 CAPLUS
CN Morpholine,
4-[[4-[[48,8aR] -4-[3,4-diethoxyphenyl]-4s,5,8,8a-tetrahydro-1oxo-2(1H)-phthalazinyl]-1-piperidinyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

449760-40-1 CAPLUS
1-Piperidineacetamide, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-(1-methylethyl)- (9CI) (CA INDEX

ANSWER 8 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

449760-48-9 CAPLUS
1(2H)-Phthalazinone, 2-{1-{2-{4-amino-3,5-dichloropheny1}-2-oxoethy1}-4-piperidiny1}-4-(3,4-dimethoxypheny1)-4a,5,8,8a-tetrahydro-, (4aS,8aR)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-49-0 CAPLUS
CN 1(2H)-Phthalazinone,
1(3.4-(inethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-[(2-oxo-3H-1-benzopyran-7-yl)methyl]-4-piperidinyl]-, (4aS,8aR)- (9CI) (CA INDEX INMEX)

L4 ANSWER 8 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

449760-50-3 CAPLUS

RN 49780-30-3 CM Morpholine, 4-[(4-[(4-8,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl)-1-piperidinyl)acetyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-51-4 CAPLUS CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(2-phenylethyl)-4-piperidinyl)-, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 8 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 449760-52-5 CAPLUS .
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(3pyridinylmethyl)-4-piperidinyl]-, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-53-6 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-(1-(2pyridinylmethyl)-4-piperidinyl]-, (4as,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 8 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 449760-54-7 CAPLUS
CN Morpholine,
4-{[4-{(4aS,8aR)-4-{3,4-diethoxyphenyl}-4a,5,8,8a-tetrahydro-1-oxo-2[iH]-phthalazinyl]-1-piperidinyl]acetyl}- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-55-8 CAPLUS
CN 1-Piperazineethanamine,
4-[14-[148, 5a8] 4-(3, 4-diethoxyphenyl)-4a,5,8,8atetrahydro-1-oxo-2(1H)-phthalazinyl)-1-piperidinyl]acetyl]-N,N-dimethyl(SCI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 8 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

RN 449760-56-9 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-48,5,8,8a-tetrahydro-2-[1-[4-(1,2,3-thiadiazol-4-yl)phenyl]methyl]-4-piperidinyl]-, (4aS,8eR)- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

449760-57-0 CAPLUS
Benzoic acid, 4-{[[4-[(4e5,8aR)-4-(3,4-dimethoxyphenyl]-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl}acetyl]amino]-, ethylester (9CI) (CA INDEX NAME)

ANSWER 8 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

449760-58-1 CAPLUS
1-Piperidineactemide, 4-[(4as,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl)- (9Cl) (CA INDEX NAME)

L4 ANSWER 9 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

lymphoid cells in combination with differentiation inducers and agents that increase cAMP levels or cAMP analogs)

RN 449760-14-9 CAPLUS

CN Piperidine,

4-[(ass,88a]-4-[3,4-diethoxyphenyl]-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-[(4-methylphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 449760-15-0 CAPLUS CN Piperidine, 4-[(4a5,8a7)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-(methylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

449760-16-1 CAPLUS
Piperidine, 1-acetyl-4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]- (9CI) (CA INDEX NAME)

Habte

L4 ANSMER 9 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:610086 CAPLUS
DOCUMENT NUMBER: 141:134659
TITLE: PDE4 inhibitors for the treatment of neoplasms of

PDE4 inhibitors for the treatment of neoplasms of lymphoid cells Hatzelmann, Armin; Tenor, Hermann; Gekeler, Volker; Sanders, Karl; Garattini, Enrico; Braunger, Juergen; Schudt, Christian Altana Pharma Ag, Germany PCT int. Appl., 78 pp. CODEN: PIXXD2 Patent INVENTOR (S) :

PATENT ASSIGNEE(S): SOURCE:

DOCUMENT TYPE:

LANGUAGE:

PAMILY ACC. NUM. COUNT: PATENT INFORMATION:

	PA	TENT	NO.		•	KIN	D	DATE	;		APPL	ICAT	ION	NO.		ם	ATE	
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	NO	2004	0626	71		A2	2004	0729		WO 2	004-	20040114						
	WO	2004	0626	71		A3		2005	0127									
		W:	AE,	AG,	AL,	AM,	AT,	AU,	AZ,	BA.	BB,	BG,	BR,	BW,	BY,	BZ,	CA,	CH,
			CN,	co,	CR,	Cυ,	CZ,	DE,	DK.	DM.	DZ.	EC.	EE.	EG.	ES.	PI,	GB,	GD,
			GE,	GH,	GM,	HR,	HU,	ID,	IL.	IN.	IS.	JP.	KE.	KG.	KP.	KR,	KZ,	LC,
			LK,	LR,	LS,	LT.	LU.	LV,	MA,	MD.	MG.	MK.	MN.	MW.	MX.	MZ		
	AU 2004204355													20040114				
	CA	2512	819			A1		2004	0729		CA 2	004 -	2512	819		2	0040	114
	EP	1587	512			A2		2005	1026		EP 2	004-	7019	02		2	0040	114
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									MK.									
	JP	2006							0525								0040	114
	US	2006	1488	04												2	0050	713
RIO		APE				,	٠					003-					0030	

OTHER SOURCE(S): MARPAT 141:134069

AB The invention relates to the use of certain PDE4 inhibitors alone or in combination with one or more differentiation inducing agents and/or an agent effective in raising intracellular concens. of cAMP or a stable analog of cAMP in the preparation of pharmaceutical compns. for the

WO 2004-EP196

analog of cAMP in the preparation or treatment of neoplasms of lymphoid cells.

IT 449760-14-9 449760-15-0 449760-16-1 449760-17-2 449760-17-2 449760-20-7 449760-21-8 449760-22-9 449760-22-3 449760-24-1 449760-24-2 449760-24-3 449760-24-1 449760-35-4 449760-30-4 449760-35-4 449760-40-1 449760-42-3 449760-53-6 449760-51-4 449760-53-6 449760-51-5 449760-53-6 449760-51-5 449760-53-6 449760-51-5 56102-07-7 596102-09-9

RL: PAC (Pharmacological activity);

SPECIAL PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (phosphodiesterase 4 (PDE4) inhibitors for treatment of neoplasms of

ANSWER 9 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

RN 449760-17-2 CAPLUS
CN 1-Piperidinepentanoic acid,
4-[(445,881)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-5-oxo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

449760-19-4 CAPLUS
1-Piperidinecarboxamide, 4-[{4aS,8aR}-4-{3,4-diethoxyphenyl}-4a,5,8,8a-tetrahydro-1-oxo-2{1H}-phthalazinyl}-N-{1,1-dimethylethyl}- (9CI) (CA INDEX NAME)

L4 ANSWER 9 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

449760-20-7 CAPLUS
1-Piperidinecarboxamide, 4-{{4aS,8aR}-4-(3,4-diethoxyphenyl}-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl}-N-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

449760-21-8 CAPLUS
1-Piperidinecarboxamide, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl)-N-(1,1-dimethylethyl)- (9CI) (CAIMDEX NAME)

Absolute stereochemistry.

L4 ANSWER 9 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

PAGE 1-A

RN 449760-24-1 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-(1-(4ntrophenyl)-4-piperidinyl)-, (4a5,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 9 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

449760-22-9 CAPLUS 1-Piperidinecarboxamide, 4-{(4aR,8aS)-4-(2,3-dihydro-7-methoxy-2,2-

dimethyl-4-benzofuranyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-(1,1-dimethylethyl)-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

449760-23-0 CAPLUS
Piperidine, 4-[(4a8,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-[[5-(dimethylamino)-1-naphthalenyl]sulfonyl]-(SCI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 9 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

RN 449760-25-2 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-{1-{4pyridinylmethyl)-4-piperidinyl]-, (4eS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-26-3 CAPLUS
CN Morpholine,
4-[(4-[(48.8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,88-tetrahydro1-oxo-2(1H)-phthalazinyl)-1-piperidinyl)carbonyl)- (9CI) (CA INDEX NAME)

RN 449760-28-5 CAPLUS
CN 1(2H)-Phthalazinone,
-(1,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(1-methyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)-4-piperidinyl]- (9CI) (CA INDEX NAME)

L4 ANSWER 9 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued I (2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(2-pyrimidinyl)-4-piperidinyl]-, (4aS,8aR)- (9CI) (CA INDEX NAME) (Continued)

Absolute stereochemistry.

RN 449760-35-4 CAPLUS
CN Morpholine,
4-[[4-[(48,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1oxo-2(1H)-phthalazinyl]-1-piperidinyl]carbonyl]- (9CI) (CA INDEX NAME)

449760-40-1 CAPLUS
1-Piperidineacetamide, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-(1-methylethyl)- (9CI) (CA INDEX NAME)

L4 ANSWER 9 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

PAGE 2-A

449760-29-6 CAPLUS 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-(1-thieno[2,3-d]pyrimidin-4-yl-4-piperidinyl)-, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

PAGE 2-A

449760-30-9 CAPLUS

L4 ANSWER 9 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN Absolute stereochemistry. (Continued)

449760-42-3 CAPLUS 2,3-Piperazinedione, 1-{[4-{(4aS,8aR)-4-{3,4-dimethoxyphenyl}-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl}-1-piperidinyl}carbonyl}-4-ethyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-47-8 CAPLUS CN Piperidine, 4-[(4as, SaR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-(4-pyridinylcarbonyl)- (9CI) (CA INDEX NAME)

449760-48-9 CAPLUS
1(2H)-Phthalazinone, 2-(1-[2-(4-amino-3,5-dichlorophenyl)-2-oxoethyl]-4-piperidinyl]-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-, (4aS,8aR)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-49-0 CAPLUS CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-[(2-oxo-2H-1-benzopyran-7-yl)methyl]-4-piperidinyl]-, (4aS,8aR)- (9CI) (CA

L4 ANSWER 9 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN Absolute stereochemistry. (Continued)

RN 449760-52-5 CAPLUS CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-{1-(3-pyridinylmethyl)-4-piperidinyl]-, (4eS,8aR)- (9CI) (CA INDEX NAME)

RN 449760-53-6 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-{1-{2pyridinylmethyl)-4-piperidinyl]-, {4aS,8aR}- {9CI} (CA INDEX NAME)

L4 ANSWER 9 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN INDEX NAME)

Absolute stereochemistry.

RN 449760-50-3 CAPLUS
CN Morpholine,
4-[[4-{[48,8aR]-4-(3,4-dimethoxyphenyl]-4a,5,8,8a-tetrahydro1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]acetyl}- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-51-4 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-{2-phenylethyl}-4-piperidinyl}-, (4aS,8aR)- (9CI) (CA INDEX NAME)

L4 ANSWER 9 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

449760-56-9 CAPLUS
1(2H)-Phthalazinone,
3,4-dimethoxyphenyll-4a,5,8,8a-tetrahydro-2-[1-[[4(1,2,3-thiadiazol-4-yl)phenyl]methyl]-4-piperidinyl)-, (4aS,8aR)- (9CI)
(CA INDEX NAME)

449760-57-0 CAPLUS
Benzoic acid, 4-[[[4-[[4as,8aR]-4-(3,4-dimethoxyphenyl]-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]acetyl]amino]-, ethyl ester (9CI) (CA INDEX NAME)

449760-58-1 CAPLUS
1-Piperidineacetamide, 4-[(4sS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 596102-01-1 CAPLUS CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(1-methylethyl)-4-piperidinyl)- (9CI) (CA INDEX NAME)

ANSWER 9 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

L4 ANSWER 9 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

596102-07-7 CAPLUS

RN 596102-07-7 CAPLUS
CN Piperidine,
4-[(448,848)-4-(3,4-diethoxyphenyl)-44,5,8,8a-tetrahydro-1-oxo2(1H)-phthalazinyl]-1-(4-morpholinylacetyl)- (9CI) (CA INDEX NAME)

RN 596102-09-9 CAPLUS
CN Piperidine, .
4-[(4aS, 8aR]-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo2(1H)-phthalazinyl)-1-[[4-{2-(dimethylamino)ethyl}-1-piperazinyl)acetyl](9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSMER 10 OF 22 CAPLUS COPYRIGHT 2007 ACS ON STN
ACCESSION NUMBER:
DOCUMENT NUMBER:
111LE:
11LE:
111LE:
11LE:

PAMILY ACC. NUM. COUNT: PATENT INFORMATION:

PATENT NO. KIND DATE APPLICA...

WO 2004018457 A1 20040304 WO 2003-EP8675 20030806 MO 2004018457 AB 20040506

W: AE, AL, AU, BA, BR, CA, CN, CO, DZ, EC, GE, HR, ID, IL, IN, IS, JP, KR, LT, LV, MA, MK, MK, NO, NZ, PH, PL, SO, TN, UA, US, VN, YU, ZA, ZW

RN: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR

CA 2494613 A1 20040314 AU 2003-258576 20030806 EP 1537100 A1 20050608 EP 2003-792157 20030806

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

BR 2003013330 A 20050614 BR 2003-13330 20030806 CN 1671695 A 20050921 CN 2003-818530 20030806 JP 2006-500370 T 20050915 CN 2003-818530 20030806 JP 2006-500370 T 2005015 JP 2004-530086 20030806 JP 2006-500370 T 2005015 JP 2004-530086 20030806 JP 2006-500370 T 2005015 JP 2004-530086 20030806 JP 20050160813 A1 20050720 US 2005-523412 20051107 A 20020810 CN 1671695 JP 2006500370 IN 2005MN00028 US 2006160813 PRIORITY APPLN. INFO.:

OTHER SOURCE(S): MARPAT 140:217652

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

1-(4-Piperidinyl)-4a,5,8,8a-tetrahydro-1H-phthalazin-1-one compds. of formula (I) [R1 and R2 are both H or together form an addnl. bond; R3 = 0 Ph derivative of formulas Q or Q1; R4 = C1-4 alkoxy or C1-4 alkoxy which

completely or predominantly substituted by fluorine; R5 = C1-4 alkoxy, C3-7 cycloalkylmethoxy, C1-4 alkoxy which is completely or predominantly substituted by fluorine; R6 = C1-4 alkoxy or C1-4 alkoxy which is completely or predominantly substituted by fluorine; wherein R7

C1-4 alkyl; R8 = H, C1-4 alkyl; or R7 and R8 together and with inclusion of the two carbon atoms, to which they are bonded, form a spiro-linked

02/09/2007

L4 ANSMER 10 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
6- or 7-membered hydrocarbon ring, optionally interrupted by an oxygen or
sulfur atom; R9 = CO(CH2)n-R10; wherein R10 = 2.5-dioxopyrrolidin-1-y]; n
= an integer of 1-4] and the salts of these compds. These compds are
useful in the prepn. of pharmaceutical compns. for the treatment of an
illness treatable by the administration of a PDB4 inhibitor, in
particular
airway disorders. Thus,
1-2-(4-(485,8aR)-4-(3,4-Dimethoxyphenyl)-1-oxo4a.5.8.8a-tetrahydro-1H-phthalazin-2-yl]piperidin-1-yl]-2oxocethyl]pyrrolidin-2-2,5-dione > . Thue, a mixt. of 1 g
(4aS.8aR)-2-(1-(2-Chloroethanoyl)piperidin-4-yl]-4-(3,4-dimethoxyphenyl)4a.5.8.8a-tetrahydro-2H-phthalazin-1-one, 0.4 g succinimide, 1 g
potamsium

#4.5.8.80 in 20 mL DMF was stirred for 18 h at room temp. to give, after workup and silica gel chromatog. and crystn. from EtOAc.

1-[2-[4-[(4aS,8aR)-4-(3,4-Dimethoxyphenyl)-1-oxo-4a,5,8,8a-tetrahydro-1H-phthalazin-2-yl]piperidin-1-yl]-2-oxoethyl]pyrrolidine-2,5-dione (II).

showed -logIC50(mol/L) of 10.66 against PDE4.

380226-97-1P, (4AS,6aR)-4-(3,4-Dimethoxyphenyl)-2-piperidin-4-yl4a,5,8,8a-tetrahydro-2H-phthalazin-1-one hydrochloride
380227-13-4P, (4AS,6aR)-4-(3,4-Diethoxyphenyl)-2-piperidin-4-yl4a,5,8,8a-tetrahydro-2H-phthalazin-1-one hydrochloride
666735-57-5P 666735-57-5P 666735-57-5P 666735-57-5P 666735-57-60-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(intermediate; preparation of pyrrolidinedione substituted
piperidine-phthalazones as cyclic nucleotide phosphodiesterase-4

inhibitors for treating airway diseases)
380226-97-1 CAPLUS
1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-(4-piperidinyl)-, monohydrochloride, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

ANSWER 10 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 666735-60-0 CAPLUS
CN 1(2H)-Phthalazinone,
(-(2,3-dihydro-7-methoxy-2,2-dimethyl-4-benzofuranyl)4a,5,8,8a-tetrahydro-2-(4-piperidinyl)-, monohydrochloride,
(4aR,8a5)-rel(SCI) (CA INDEX NAME)

Relative stereochemistry.

● HC1

666735-56-4P RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (preparation of pyrrolidinedione substituted piperidine-phthalazones L4 ANSWER 10 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

● HC1

380227-13-4 CAPLUS 1(3H)-Phthalazinone, 4-(3,4-diethoxyphenyl)-4m,5,8,8m-tetrahydro-2-(4-piperidinyl)-, monohydrochloride, (4mS,8mR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

• HC1

666735-57-5 CAPLUS
Piperidine, 1-(chloroacetyl)-4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]- (9CI) (CA INDEX NAME)

ANSWER 10 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued) cyclic nucleotide phosphodiesterase-4 (PDE4) inhibitors for treating airway diseases) 666735-56-4 CAPLUS Piperidine, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl)-1-[(2,5-dioxo-1-pyrrolidinyl)acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

REFERENCE COUNT:

THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

10/523,111

Page 43

L4 ANSMER 11 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:182864 CAPLUS

140:217651 140:217651

INVENTOR(S): Hatzelmenn, Armin, Bareig, Johannes Marx, Degenhard; Kley, Hans-Peter; Christians, Johannes A. M.; Menge, Wiro M. P. B.; Sterk, Geert Jan

Altana Pharma A.-G., Germany

POT Int. Appl., 52 pp.

CODEN: PIXXD2

Patent

Patent

DOCUMENT TYPE: LANGUAGE: English

FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

	PAT	TENT	NO.			KIN	D	DATE			APPL	ICAT	ION	NO.		D	ATE	
		. 					-									-		
	WO	2004	0184	51		Al		2004	0304	1	WO 2	003-	EP86	77		2	0030	806
	WO	2004	0184	51		A8		2004	0506									
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OTHER SOURCE(S): MARPAT 140:217651

$$R^3$$
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Title compds. {I; R1, R2 = H, alkyl; R3 = Q1, Q2; R4 = (fluoro)alkoxy;

ANSWER 11 OF 22 CAPLUS COPYRIGHT 2007-ACS on STN (Continued) L4

666750-57-8 CAPLUS 3(2H)-Pyridazinone, 4-dimethoxyphenyl)-4,5-dihydro-2-(4-piperidinyl)-, monohydrochloride (9CI) (CA INDEX NAME)

● HC1

RN 666750-58-9 CAPLUS
CN 3(2H)-Pyridazinone,
6-(2,3-dihydro-7-methoxy-2,2-dimethyl-4-benzofuranyl)4,5-dihydro-2-(4-piperidinyl)-, monohydrochloride (9CI) (CA INDEX NAME)

● HCl

RN 666750-59-0 CAPLUS CN Piperidine, 1-acctyl-4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-4-methyl-6-oxo-1(4H)-pyridazinyl)- (9CI) (CA INDEX NAME)

L4 ANSWER 11 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

R6 = cycloalkoxy, cycloalkylmethoxy, (floorolalkoxy; R7 = alkyl; R8 = H,
alkyl; R7R8 = atoma to form a 5-7 membered ring optionally interrupted by
O, S; R9 = alkyl, SO2R10, COR13, aryl, etc.; R10 = alkyl,
S-dimethyleminonaphthalen-1-yl, thienyl, NR16R17, (substituted) Ph, etc.;
R13 = alkyl, carboxyalkyl, Ph, pyridyl, NR16R17, etc.; R16 = H, alkyl,
cycloalkylmethyl, (substituted) Ph; R17 = alkyl, cycloalkylmethyl, (substituted) Ph; R17 = alkyl, cycloalkylmethyl, (substituted) Ph; R17 = alkyl, cycloalkyl,
cycloalkylmethyl, (substituted) Ph; NR16R17, etc.; R16 = H, alkyl,
cycloalkylmethyl, (substituted) Ph; NR16R17 = 4-morpholinyl,
1-pyrrolidinyl, 1-piperidinyl, 1-hexahydroacepinyl, (substituted)
piperazinyl), were prepd. Thue, piperidin-4-ylhydrazine dihydrochloride
[Drepn. given), 4-(3, 4-dimethoxyphenyl)-3-methyl-4-oxobutyric acid, and
EtlN were refluxed 18 h in PrOH to give
6-(3,4-dimethoxyphenyl)-5-methyl-2-piperidin-4-yl-4,5-dihydro-3H-pyridazin-3-one hydrochloride. I inhibited
PDE4 with -log ICSO = 7,17-8.39.

166750-56-7P, 6-(3,4-Dimethoxyphenyl)-5-methyl-2-piperidin-4-yl-4,5-dihydro-3H-pyridazin-3-one hydrochloride 666750-57-8P
666750-66-79-666750-62-5P 666750-60-3P
666750-61-P 666750-62-5P 666750-69-P
666750-76-1P 666750-74-9P 666750-72-7P
666750-76-1P 666750-74-9P 666750-72-7P
666750-76-1P 666750-74-9P 666750-78-3P
666750-76-1P 666750-74-9P 666750-78-3P
666750-82-9P 666750-80-7P 666750-78-3P
666750-82-9P 666750-80-7P 666750-78-3P
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666750-82-9P 666750-78-9P 666750-78-3P
666750-82-9P 666750-86-1P 666750-78-3P
666750-82-9P 666750-80-7P 666750-78-3P
666750-82-9P 666750-80-7P 666750-78-3P
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666750-82-9P 666750-80-7P 666750-78-3P
666750-82-9P 666750-78-3P
666750-82-9P 666750-80-7P 666750-78-3P
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666750-82-9P 666750-80-7P 666750-78-3P
666750-82-9P

/4
inhibitors)
666750-56-7 CAPLUS
3 (2H) -Pyridazinone, 6-(3,4-dimethoxyphenyl)-4,5-dihydro-5-methyl-2-(4-piperidinyl)-, monohydrochloride (9CI) (CA INDEX NAME)

● HCl

ANSWER 11 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

666750-60-3 CAPLUS
Morpholine, 4-[[4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-4-methyl-6-oxo-1(4M)-pyridazinyl]-1-piperidinyl]carbonyl]- (9CI) (CA INDEX NAME)

666750-61-4 3(2H)-Pyrid CAPLUS

3(2H)-Pyridazinone, 6-{3,4-dimethoxyphenyl}-4,5-dihydro-5-methyl-2-[1-(3-pyridinylmethyl)-4-piperidinyl]-, dihydrochloride (9CI) (CA INDEX NAME)

●2 HC1

666750-62-5 CAPLUS
2,3-Pipersrinedione, 1-[[4-(3-(3,4-dimethoxyphenyl)-5,6-dihydro-6-oxo-1(4H)-pyridazinyl)-1-piperidinyl]carbonyl]-4-ethyl- (9Cl) (CA INDEX NAME)

10/523,111

Page 44

L4 ANSWER 11 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 666750-63-6 CAPLUS
CN Piperazine, 1-[(4-(3-(3,4-dimethoxyphenyl)-5,6-dihydro-6-oxo-1(4H)pyridazinyl)-1-piperidinyl]carbonyl]-4-methyl-, monohydrochloride (9CI)
(CA INDEX NAME)

• HC

RN 666750-64-7 CAPLUS
CN Piperidine, 4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-6-oxo-1(4H)pyridazinyi]-1-[[5-(dimethylamino)-1-naphthalenyl]sulfonyl]- (9CI) (CA
INDEX NAME)

L4 ANSWER 11 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN {Continued}

RN 666750-67-0 CAPLUS
CN Piperidine, 4-(3-(3,4-dimethoxyphenyl)-5,6-dihydro-6-oxo-1(4H)-pyridazinyl)-1-(methylsulfonyl)- (9CI) (CA INDEX NAME)

RN 666750-68-1 CAPLUS
CN Piperidine, 1-[(4-chlorophenyl)sulfonyl]-4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-6-oxo-1(4H)-pyridazinyl]- (9CI) (CA INDEX NAME)

RN 666750-69-2 CAPLUS
CN Piperidine, 4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-6-oxo-1(4H)pyridaxinyll-1-([phenylmethyl]sulfonyll- (9CI) (CA INDEX NAME)

L4 ANSWER 11 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 666750-65-8 CAPLUS
CN Morpholine, 4-[[4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-6-oxo-1(4H)pyridazinyl}-1-piperidinyl]acetyl]-, monohydrochloride (9CI) (CA INDEX
NAME)

● HCI

RN 666750-66-9 CAPLUS
CN Piperidine, 4-{3-(3,4-dimethoxyphenyl)-5,6-dihydro-6-oxo-1(4H)-pyridazinyl]-1-[(4-methylphenyl)aulfonyl]- (9CI) (CA INDEX NAME)

L4 ANSWER 11 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 666750-70-S CAPLUS
CN Piperidine, 4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-6-oxo-1(4H)pyridazinyl)-1-[(4-methoxyphenyl)aulfonyl)- (9Cl) (CA INDEX NAME)

RN 666750-71-6 CAPLUS
CN Piperidine, 4-{3-(3,4-dimethoxyphenyl)-5,6-dihydro-6-oxo-1{4H}-pyridazinyl}-1-{phenylsulfonyl}- (9CI) (CA INDEX NAME)

RN 666750-72-7 CAPLUS
CN Piperidine, 4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-6-oxo-1(4H)pyridazinyl)-1-(1(3,5-dimethoxyphenyl)sulfonyl)- (9CI) (CA INDEX NAME)

MéO OME

RN 666750-73-8 CAPLUS
CN Piperidine, 1-[{2-cyanophenyl}sulfonyl]-4-{3-(3,4-dimethoxyphenyl)-5,6-dihydro-6-oxo-1(4H)-pyridazinyl}- (9CI) (CA INDEX NAME)

Meo Meo

RN 666750-74-9 CAPLUS
CN Piperidine, 4-{3-(3,4-dimethoxyphenyl)-5,6-dihydro-6-oxo-1(4H)-pyridazinyl)-1-(2-thienylsulfonyl)- (9CI) (CA INDEX NAME)

Meo Ne s s

RN 666750-75-0 CAPLUS
CN Piperidine, 4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-6-oxo-1(4H)-pyridazinyl}-1-[(2-fluorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

L4 ANSWER 11 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

Ph OMe

RN 666750-79-4 CAPLUS
CN Piperidine, 4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-6-oxo-1(4H)-pyridazinyl]-1-(3-pyridinylcarbonyl)- (9CI) (CA INDEX NAME)

Meo OMe

RN 666750-80-7 CAPLUS
CN Piperidine, 4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-6-oxo-1(4H)-pyridazinyl)-1-(2,4,6-trichlorobenzoyl)- (9CI) (CA INDEX NAME)

Med C1 C1 C1

RN 666750-81-8 CAPLUS
CN 1-Piperidinecarboxemide, 4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-6-oxo-1(4H)-pyridaxinyll-N-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)

L4 ANSWER 11 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

Med N O

RN 666750-76-1 CAPLUS
CN Piperidine, 4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-6-oxo-1(4H)pyridazinyl)-1-[[2-(trifluoromethoxy)phenyl]sulfonyl]- (9CI) (CA INDEX
NAME)

Meo. N. S. CF3

RN 666750-77-2 CAPLUS
CN 1-Piperidinesulfonamide, 4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-6-oxo-1(4H)-pyridazinyl)-N,N-dimethyl- (9CI) (CA INDEX NAME)

O NMe2

RN 666750-78-3 CAPLUS
CN Piperidine, 1-benzoyl-4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-6-oxo-1(4H)-pyridazinyl)- (9CI) (CA INDEX NAME)

L4 ANSWER 11 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

NHBu - t

RN 666750-82-9 CAPLUS
CN 1-Piperidineacetamide,
4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-6-oxo-1(4H)pyridazinyl)-N,N-dimethyl-, monohydrochloride (9CI) (CA INDEX NAME)

Me₂N-C-CH₂

• HCl

RN 666750-83-0 CAPLUS
CN Piperazine, 1-[[4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-6-oxo-1(4H)-pyridazinyl]-1-piperidinyl]acetyl]-4-methyl-, dihydrochloride (9CI) (CA INDEX NAME)

ANSWER 11 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

666750-84-1 CAPLUS
Piperidine, 4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-6-oxo-1(4H)pyridazinyl]-1-[4-(4-pyridinyl)-1-piperazinyl]acetyl]-, dihydrochloride
(9CI) (CA INDEX NAME)

●2 HCl

666750-85-2 CAPLUS
Piperidine, 4-[3-(3, 4-dimethoxyphenyl)-5,6-dihydro-6-oxo-1(4H)pyridazinyl]-1-[4-(2-methoxyphenyl)-1-piperazinyl]acetyl]-,
dihydrochloride (9CI) (CA INDEX NAME)

ANSWER 11 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

REFERENCE COUNT

THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L4 ANSWER 11 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

●2 HC1

666750-86-3 CAPLUS
Piperidine, 4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-6-oxo-1(4H)-pyridazinyl]-1-[4-(diphenylmethyl)-1-piperazinyl]acetyl]-,
dihydrochloride (9CI) (CA INDEX NAME)

666750-88-5P RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation of piperidinylpyridazinones as phosphodiesterase PDE4 or

PDE3/4
inhibitore)

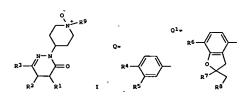
RN 666750-88-5 CAPLUS
CN Piperidine,
1-(chloroacety!)-4-{3-(3,4-dimethoxypheny!)-5,6-dihydro-6-oxo1(4H)-pyrideziny!}- (9CI) (CA INDEX NAME)

DOCUMENT TYPE: LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

	PA7	FENT	N	ю.			KIN	D	DATE			APPL	ICAT	ION	NO.		D.	ATE	
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	WO	200	40	184	50		A1		2004	0304		WO 2	003-	EP86	76		2	0030	806
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		RW	:	AM.	AZ.	BY.	KG.	KZ.	MD.	RU.	TJ.	TM,	AT.	BE.	BG.	CH.	CY.	CZ.	DE.
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												MO 3	UU3 -	5F86	,,		- 4	UU30	006

OTHER SOURCE(S):

MARPAT 140:235730



The 1,2-dihydro-2- $\{1-xidopiperidin-4-yl\}$ phthalazin-2-one derivs. $\{I; R1, R2 = H, C1-4 alkyl; or R1 and R2 together and with inclusion of the two$

ANSMER 12 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued) carbon atoms, to which they are bonded, form a group selected from cyclohexane-1,2-diyl or 4-cyclohexene-1,2-diyl, R3 = a Ph deriv. of formulas Q or Q1; R4 = C1-4 alkoxy or C1-4 alkoxy which is completely or predominantly substituted by fluorine; R5 = C1-8 alkoxy, C3-7 cycloalkylmethoxy, C1-4 alkoxy which is completely or predominantly substituted by fluorine; R6 = C1-4 alkoxy, C3-5 cycloalkylmethoxy, C1-4 alkoxy which is completely or predominantly substituted by fluorine; R7 = C1-4 alkyl; R8 = H, C1-4 alkyl; or wherein R7 and R8 together and with inclusion of the two carbon atoms, to which they are bonded, form a spiro-linked 5-, 6- or 7-membered hydrocarbon ring, optionally interrupted by an oxygen or sulfur atom; R9 = (C12)mSO2R10, (CH2)nCOR11, -(CH2)p-2-(CH2)q-R14; wherein R10, R11 = N(R12)R13; R12, R13 = H, C1-7 alkyl, C3-7 cycloalkyl, C3-7 cycl

O, CO, CONH, NHCO, SO2; R14 = H, OH, C1-4 alkoxy, hydroxy-C2-4 alkoxy, C1-4 alkoxy-C1-4 alkoxy, C1-4 alkoxy-C1-4 a

Dimethoxy)phenyl]-1-oxo-4a,5,8,8a-tetrahydro-1H-phthalazin-2-yl]piperidin-1-yl-2H-acetamide hydrochloride in 100 mL CH2Cl2 was washed with aq. satd.

NaHCO3 soln., dried over anhyd. MgSO4, cooled to 0°, treated with 0.6 g 3-chloroperbenzoic acid (70% purity), and stirred for 60 min to give, after workup and silica gel chromatog. and crystn. from EtOA., 2-(4-[(48S, 8aR]-4-[3,4-Dimethoxyphenyl]-1-oxo-4a,5,6,8a-terhahydro-1H-phthalazin-2-yl]-1-oxypiperidin-1-yl]acetamide (II). II and 2-(4-[(48S, 8aR]-4-[3,4-Dimethoxyphenyl]-1-oxo-4a,5,6,8a-tetrahydro-1H-phthalazin-2-yl]-1-oxypiperidin-1-yl]-N-isopropylacetamide showed IC50

(4AS, 8aR)-4-(3,4-Dimethoxyphenyl)-2-piperidin-4-yl-4a,5,6,7,8,8a-hexahydro-2H-phthalazin-1-one hydrochloride RL: RCT (Reactant): SFN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (intermediate; preparation of piperidine N-oxide derivs. as phosphodiesterase 4 (PDE4) inhibitors for treating airway disorders) RN 380226-97-1 CAPLUS CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-(4-piperidinyl)-, monohydrochloride, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

ANSWER 12 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

449760-44-5 CAPLUS
1-Piperidineacetamide, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl)-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry

● HCl

RN 666735-60-0 CAPLUS
CN 1(2H)-Phthalaxinone,
4-(2,3-dimydro-7-methoxy-2,2-dimethyl-4-benzofuranyl)4a,5,8,8a-tetrahydro-2-(4-piperidinyl)-, monohydrochloride,
(4aR,8aS)-rel(9C1) (CA INDEX NAME)

Relative stereochemistry.

L4 ANSWER 12 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

● HC1

380227-13-4 CAPLUS
1(2H)-Phthalazinone, 4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-2-(4-piperidinyl)-, monohydrochloride, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

• HCl

449760-40-1 CAPLUS
1-Piperidineacetamide, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-(1-methylethyl)- (9CI) (CA INDEX

ANSWER 12 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

• HCl

RN 666748-55-6 CAPLUS
CN 1-Piperidineacetamide,
4-(4as, 8as)-4-(3,-4 dimethoxyphenyl)-4a,5,6,7,8,8ahexahydro-1-oxo-2(1H)-phthalazinyl]-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

• HC1

666748-56-7 CAPLUS
1(2H)-Phthalarinone,
4-dimethoxyphenyl)-4a,5,6,7,8,8a-hexahydro-2-(4piperidinyl)-, monohydrochloride, (4aS,8aR)- (9CI) (CA INDEX NAME)

02/09/2007

● HCl

666854-35-9P 666854-37-1P 666854-40-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(preparation of piperidine N-oxide derivs. as phosphodiesterase 4 (PDE4)

inhibitors for treating airway disorders)
666854-35-9 CAPLUS
1-Piperidineacetamide, 4-[(4a5,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-, 1-oxide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

666854-37-1 CAPLUS

L4 ANSMER 12 OF 22 CAPLUS COPYRIGHT 2007 ACS ON STN (Con CN 1-Piperidineacetamide, 4-[(4a5, Baf) -4-(3, 4-dimethoxyphenyl)-4a,5,6,7,8,8a-hexahydro-1-oxo-2(1H)-phthalazinyl)- (9CI) (CA INDEX NAME) (Continued)

Absolute stereochemistry.

REFERENCE COUNT:

THERE ARE 10 CITED REFERENCES AVAILABLE FOR

RECORD. ALL CITATIONS AVAILABLE IN THE RE

ANSWER 12 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
1-Piperidineacetamide, 4-[(4eS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-(1-methylethyl)-, 1-oxide (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

666854-40-6 CAPLUS

CN 1-Piperidineacetamide, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,6,7,8,8a-hexahydro-1-oxo-2(1H)-phthalazinyl]-, 1-oxide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

IT 666748-54-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; preparation of piperidine N-oxide derivs. as
phosphodiesterase 4
(PDE4) inhibitors for treating airway disorders)
RN 666748-54-5 CAPLUS

L4 ANSWER 13 OF 22 CAPLUS COPYRIGHT 2007 ACS ON STN ACCESSION NUMBER: 2004:182862 CAPLUS DOCUMENT NUMBER: 140:217665

Preparation of piperidinylphthalazinone derivatives TITLE:

PDE4 inhibitors
Hatzelmann, Armin, Barsig, Johannes; Marx, Degenhard;
Kley, Hans-Peter; Christiaans, Johannes A. M.; Menge,
Wiro M. P. B.; Sterk, Geert Jan; Weinbrenner, Steffen
Altans Pharms A.-G., Germany
PCT Int. Appl., 48 pp.
CODEN: PIXXD2
Patent
English
1 INVENTOR (S):

PATENT ASSIGNEE(S): SOURCE:

DOCUMENT TYPE:

FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

MO 2004018449 A1 20040304 WO 2003-EP8673 20030806
MO 2004018449 A8 20040506
M: AE, AL, AU, BA, AR, CA, CN, CO, DZ, EC, GE, HR, ID, IL, IN, IS,
JP, KR, LT, LV, MA, MK, MX, NO, NZ, PH, PL, SG, TN, UA, US, VN,
YU, ZA, ZW

RM: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE,
DK, EE, ES, PI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE,
SI, SK, TR
AU 2003255376 A1 20040311 AU 2003-255376 200300000 WO 2003-EP8673 W 20030806

OTHER SOURCE(S): MARPAT 140:217665

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

The title compound I $[R1, R2 = H \text{ or together form an addnl. bond; } R3 = benzene derivative Q1 or Q2; R4 = <math>\{substituted\}$ arylsulfonyl; R5 = alkoxy

polyfluoroaikyoxy; R6, R7 = (cyclo)alkoxy, cycloalkylmethoxy, or polyfluoroaikyoxy; R8 = alkyl; R9 = H or alkyl; or R7 and R8 together with

the 2 intervening C atoms form a spiro-linked 5-, 6- or 7-membered hydrocarbon ring, optionally interrupted by 0 or 5] were prepared as PDE4 inhibitors. Thus, reaction of (4sS,8aR)-4-(1,4-dimethoxyphenyl)-2-piperidin-4-yl-4a-,5.8.8a-tetrahydro-2H-phthalazin-1-ome hydrochloride (preparation given) with naphthalane-1-aulfonyl chloride gave compound

The prepared compds. inhibited PDE4 with -log(IC50) ≥ 8.8.
666737-07-1P 666737-09-3P 666737-10-6P
666737-11-7P 666737-12-8P 666737-13-9P
666737-14-0P 666737-15-1P 666737-16-2P
666737-12-3P 666737-18-4P 666737-19-5P
666737-20-8P 666737-21-9P 666737-22-0P
666737-23-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU

ANSMER 13 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued) (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (prepn. of piperidinylphthalazinone derivs. as PDE4 inhibitors) 666737-07-1 CAPLUS Piperidine. 4-[(465.8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl}-1-(1-naphthalenylsulfonyl)- (9CI) (CA INDEX)

Absolute stereochemistry.

666737-09-3 CAPLUS
Piperidine, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1oxo-2(1H)-phthalazinyl]-1-[(phenylmethyl)sulfonyl]- (9CI) (CA INDEX

Absolute stereochemistry.

L4 ANSWER 13 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

666737-12-8 CAPLUS
Piperidine, 4-(448,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1oxo-2(1H)-phthalazinyl]-1-(2-thienylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

666737-13-9 CAPLUS
Piperidine, 4-{(4aS,8aR)-4-{3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl)-1-{(3,5-dimethyl-4-isoxazolyl)sulfonyl}- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 13 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

666737-10-6 CAPLUS
Piperidine, 1-[(5-chloro-1,3-dimethyl-1H-pyrezol-4-yl)sulfonyl]-4[(465,867,4-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthelezinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

666737-11-7 CAPLUS
Piperidine, 4-(4483,8aR)-4-(3,4-dimethoxyphenyl)-4e,5,8,8a-tetrahydro-1oxo-2(1H)-phthalazinyl)-1-(8-quinolinylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 13 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

666737-14-0 CAPLUS
Piperidine, 1-[(5-chloro-2-thienyl)sulfonyl]-4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl)- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

666737-15-1 CAPLUS
Piperidine, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-cxo-2(1H)-phthalazinyl]-1-[[2-(trifluoromethoxy)phenyl]sulfonyl]- (9CI)
(CA INDEX NAME)

RN 666737-16-2 CAPLUS
CN 3-Thiophenecarboxylic acid, 5-[[4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tertahydro-1-oxo-2(1H)-phthalazinyl)-1-piperidinyl)sulfonyl]-4-methoxy-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 666737-17-3 CAPLUS
CN Piperidine, 4-[(4aS, BaR)-4-(3,4-dimethoxyphenyl)-4a,5,8,Ba-tetrehydro-1oxo-2(IH)-phthalazinyl]-1-[[4-(phenylsulfonyl)-2-thienyl]sulfonyl)- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 13 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 666737-20-8 CAPLUS
CN Piperidine, 1-[(4,5-dichloro-2-thienyl)sulfonyl]-4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 666737-21-9 CAPLUS
CN Piperidine,
1-[(5-chloro-3-methylbenzo[b]thien-2-yl]sulfonyl]-4-[(4aS,8aR)4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl](9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 13 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 666737-18-4 CAPLUS
CN Benzamide, N-[[5-[[4-[[(4as,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]sulfonyl]-2-thienyl]methyl]- (9Cl) (CA INDEX NAME)

Absolute stereochemistry.

RN 666737-19-5 CAPLUS
CN Piperidine, 4-[(4aS.8aR)-4-{3,4-dimethoxyphenyl}-4a,5,8,8a-tetrahydro-1oxo-2(1H)-phthalazinyl}-1-{{5-(3-isoxazolyl)-2-thienyl}sulfonyl}-(9CI)
(CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 13 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 666737-22-0 CAPLUS
Piperidine, 4-[(4as,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-[[5-(2-pyridinyl)-2-thienyl]sulfonyl]- (9CI)
(CA INDEX NAME)

Absolute stereochemistry

RN 666737-23-1 CAPLUS

Piperidine, 4-[(465,88R)-4-(3,4-dimethoxyphenyl]-48,5,8,8a-tetrahydro-1oxo-2(1H)-phthalazinyl]-1-[[4-(trifluoromethoxy)phenyl]sulfonyl]- (9CI)
(CA INDEX NAME)

180226-97-1P 380227-13-4P 666735-60-0P RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation of piperidinylphthalazinone derive. as PDE4 inhibitors) 380226-97-1 CAPLUS (2AH)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-(4-piperidinyl)-, monohydrochloride, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

• HC1

380227-13-4 CAPLUS 1(2H)-Phthalazinone, 4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-2-(4-

ANSWER 13 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

REFERENCE COUNT:

THERE ARE 13 CITED REFERENCES AVAILABLE FOR

FORMAT

RECORD. ALL CITATIONS AVAILABLE IN THE RE

(Continued)

ANSWER 13 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued) piperidinyl)-, monohydrochloride, (4as,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

● HCl

RN 666735-60-0 CAPLUS
CN 1(2H)-Phthalazinone,
4-(2,3-dihydro-7-methoxy-2,2-dimethyl-4-benzofuranyl)4a,5,8,8a-tetrahydro-2-(4-piperidinyl)-, monohydrochloride,
(4aR,8a8)-rel(9CI) (CA INDEX NAME)

Relative stereochemistry.

L4 ANSWER 14 OF 22 CAPLUS COPYRIGHT 2007 ACS ON STN ACCESSION NUMBER: 2004:182711 CAPLUS DOCUMENT NUMBER: 140:225729 TITLE: Preparation 140:235729
Preparation of piperidine-substituted pyridazones and phthalazones as PDE4 inhibitors
Sterk, Geert Jan; Hatzelmann, Armin; Marx, Degenhard; Kley, Hans-Peter; Menge, Wiro M. P. B.
Altana Pharma A.-G., Germany
PCT Int. Appl., 65 pp.
CODEN: PIXXD2
Patent

INVENTOR(S):

PATENT ASSIGNEE(S): SOURCE:

DOCUMENT TYPE:

Patent English LANGUAGE:

FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

PAT	PATENT NO.					KIND DATE				APPL	I CAT	ION	NO.	DATE				
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WO	2004	0179	74	•	A1		2004	0304		WO 2	003-	EP87	24		2	0030	806	
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			ZA,															
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CA	2494	634			Al		2004	0304		CA 2	003-	2494	634		2	0030	806	
AU	2003	2603	76		A1		2004	0311		AU 2	003-	2603	76		2	0030	806	
EP	1556	049			Al		2005	0727		EP 2	003-	7922	67		2	0030	806	
		AT,																
										AL.								
JP	2005									JP 2								
US	2006	0947																
RIORITY										EP 2								
										WO 2	003-	EP87	24	,	W 2	0030	806	

OTHER SOURCE(S): MARPAT 140:235729

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Title compds. I [R1-2 = H, alkyl, etc.; R3 = substituted Ph, etc.; R9 = naphthyl, pyrazinyl, pyridazinyl, etc.] are prepared For instance,

(4aS, 8aR) -4 - (3, 4-Dimethoxyphenyl) -2-piperdin-4-yl-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one hydrochloride (preparation given) is reacted with methanesulfonylscetic acid (CH2Cl2, Et3N) to give II. Compds. of the invention have plCSO ≥ for the PDE4 receptor. I are useful for the treatment of sirway disorders.

IT 666851-01-0P, (4AS,8aR)-2-{1-{3-(2-aminoethanesulfonyl)propanoyl)p

iperidin-4-yl]-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2H-phthalazin-

1-one
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); TRU (Therapeutic use); BIOL (Biological atudy); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of piperidine-substituted pyridasones and phthalazones as PDE4

02/09/2007

ANSWER 14 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued) inhibitors)
666851-01-0 CAPLUS
Piperidine,
- [(2-aminoethyl) sulfonyl]-1-oxopropyl]-4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]- [9CI]
(CA INDEX NAME)

Absolute stereochemistry

IT 380227-17-8P, (4AS,8aR)-2-[1-[3-[(2-Aminoethyl)sulfanyl]propanoyl]

1,2-dihydroquinolin-6-yl)oxy|butanoyl|piperidin-4-yl|-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one 666851-07-6P, (4AS,8aR)-2-[1-[2-(2-Aninoethoxy)ethyl]piperidin-4-yl]-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one dihydrochloride 666851-10-1P, (4AS,8aR)-4-(3,4-Dimethoxyphenyl)-2-[1-(2-methoxyethyl)piperidin-4-yl]-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one hydrochloride 666851-12-3P, (4AS,8aR)-4-(3,4-Dimethoxyphenyl)-2-[1-(2-methyl)piperidin-4-yl]-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one hydrochloride 666851-13-6P, (4AS,8aR)-4-(3,4-

Dimethoxyphenyl) -2-{1-{2-(methanesulfonyl)ethyl)piperidin-4-yl]-4a,5,8,8a-

ANSWER 14 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued) tetrahydro-2H-phthalazin-1-one hydrochloride 666851-17-8P,

(4AS, 8aR)-4-(3,4-Dimethoxyphenyl)-2-[1-[2-(2-hydroxyethoxy)ethyl]piperidin-4-yl]-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one 666851-19-0P,
6-[4-[4-(3,4-Dimethoxyphenyl)-6-0x0-5,6-dihydro-4H-pyridazin-1yl]piperidin-1-yl]1-4-oxobutoxyl-1H-quinolin-2-one 666851-37-2P,
(4AS, 8aR)-2-[1-(2-(2-Aminoethoxy)ethyl]piperidin-4-yl]-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USRS
(Uses)

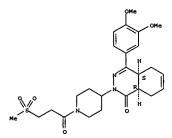
(Uses)
(prepn. of piperidine-substituted pyridazones and phthalazones as PDE4
inhibitors)
380227-17-8 CAPLUS
Piperidine, 1-[3-[(2-aminoethyl)thio]-1-oxopropyl]-4-[(46S,8aR)-4-(3,4dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

66880-88-0 CAPLUS
Piperidine, 4-[{4eS,8aR}-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl)-1-[3-(methylsulfonyl)-1-oxopropyl)- (9CI) (CA

Absolute stereochemistry.

ANSWER 14 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



666850-90-4 CAPLUS
1(2H)-Phthalazinone,
-[2-(2-benzofuranyl)-2-oxoethyl]-4-piperidinyl]-4(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-, (4aS,8aR)- (9CI) (CA INDEX NAME)

666850-93-7 CAPLUS
1(2H)-Phthalazinone, 2-{1-{{4-(1H-benzimidazol-1-yl}phenyl}methyl}-4-piperidinyl}-4-(1,4-dimethoxyphenyl)-4a,5.8,8a-tetrahydro-, monohydrochloride, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

(Continued) .

ANSWER 14 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

• HC1

666850-96-0 CAPLUS 2H-1,4-Benzoxazin-3(4H)-one, 6-[[4-[[4a5,8aR]-4-(3,4-dimethoxyphenyl]-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]acetyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

666850-99-3 CAPLUS
4-Morpholinecarboxamide, N-[2-[[]-[4-[(4as,8aR)-4-(3,4-dimethoxyphenyl)-4,5,8,8a-tetrahydro-1-oxo-2(IH)-phthalazinyl]-1-piperidinyl]-3-oxopropyl]sulfonyl]ethyl]- (9CI) (CA INDEX NAME)

RN 666851-03-2 CAPLUS
CN Piperidine,
1-[[(1,2-dihydro-2-oxo-6-quinoliny1)oxy]acety1]-4-[(4aS,8aR)-4(3,4-dimethoxypheny1)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalaziny1](9CI) (CA INDEX NAME)

Absolute stereochemistry.

666851-05-4 CAPLUS
Piperidine, 1-{4-{(1,2-dihydro-2-oxo-6-quinolinyl)oxy}-1-oxobutyl}-4((4aS,BaR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)phthalazinyl]- (9C1) (CA INDEX NAME)

ANSWER 14 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN INDEX NAME) (Continued)

Absolute stereochemistry

• HCl

RN 666851-12-3 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-[2[methylthio|ethyl]-4-piperidinyl]-, monohydrochloride, (4aS,8aR)- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

• HC1

RN 666851-15-6 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-[2-

Habte

L4 ANSWER 14 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN Absolute stereochemistry. (Continued)

666851-07-6 CAPLUS
1(2H)-Phthalazinone, 2-[1-[2-(2-aminoethoxy)ethyl]-4-piperidinyl]-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-, dihydrochloride, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

●2 HC1

RN 666851-10-1 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-{1-(2methoxyethyl)-4-piperidinyl]-, monohydrochloride, (4aS,8aR)- (9CI) (CA

ANSWER 14 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued) (methylaulfonyl)ethyl)-(-piperidinyl)-, monohydrochloride, (4aS,8aR)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

• HCl

RN 666851-17-8 CAPLUS
CN 1(2H)-Phthalazinone,
-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrehydro-2-[1-[2(2-hydroxyethoxy)ethyl]-4-piperidinyl]-, (4eS,8aR)- (9CI) (CA INDEX

Absolute stereochemistry.

666851-19-0 CAPLUS
Piperidine, 1-[4-{1,2-dihydro-2-oxo-6-quinolinyl}oxy}-1-oxobutyl}-4-[3-(3,4-dinethoxyphenyl)-5,6-dihydro-6-oxo-1(4H)-pyridazinyl}- (9CI) (CA INDEX NAME)

02/09/2007

666851-37-2 CAPLUS
1(2H)-Phthalszinone, 2-[1-[2-(2-aminoethoxy)ethyl]-4-piperidinyl]-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-, (4a5,8aR)- [9C1] (CA INDEX NAME)

Absolute stereochemistry.

380226-97-1P, (4AS,8aR)-4-(3,4-Dimethoxyphenyl)-2-(piperidin-4-yl)4a,5,8,8a-tetrahydro-2H-phthalazin-1-one hydrochloride
380227-13-4P, (4AS,8aR)-4-(3,4-Diethoxyphenyl)-2-piperidin-4-yl4a,5,8,8a-tetrahydro-2H-phthalazin-1-one hydrochloride
666735-60-0P 666730-56-7P, 6-(3,4-Dimethoxyphenyl)-5methyl-2-(piperidin-4-yl)-4,5-dihydro-2H-pyridazin-3-one hydrochloride
666750-57-6P, 6-(3,4-Dimethoxyphenyl)-2-(piperidin-4-yl)-4,5dihydro-2H-pyridazin-3-one hydrochloride 666750-58-9P,
6-(7-Methoxy-2,2-dimethyl-2,3-dihydrobenzofuran-4-yl)-2-(piperidin-4-yl)4,5-dihydro-2H-pyridazin-3-one hydrochloride
RL: RCT (Reactant): SPN (Synthetic preparation): PREP (Preparation): RACT
(Reactant or reagent)
(preparation of piperidine-substituted pyridazones and phthalazones as PDE4

DE4 inhibitore) 380226-97-1 CAPLUS 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-(4-

L4 ANSWER 14 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Con CN 1(2H)-Phthalazinone, (Con 1(2H)-Phthalazinone, (Con 4(2,3-dihydro-7-methoxy-2,2-dimethyl-4-benzofuranyl)-4a,5,8,8a-tetrahydro-2-(4-piperidinyl)-, monohydrochloride, (4aR,8aS)-rel-{9CI} (CA INDEX NAME) (Continued)

Relative stereochemistry.

• HCl

666750-56-7 CAPLUS 3(2H)-Pyridaginone, 6-(3,4-dimethoxyphenyl)-4,5-dihydro-5-methyl-2-(4-piperidinyl)-, monohydrochloride (9CI) (CA INDEX NAME)

● HC1

RN 666750-57-8 CAPLUS
CN 3 (2H)-Pyridazinone,
6-(3,4-dimethoxyphenyl)-4,5-dihydro-2-(4-piperidinyl), monohydrochloride (9CI) (CA INDEX NAME)

ANSWER 14 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued) piperidinyl)-, monohydrochloride, (4aS,8aR)-.(9CI) (CA INDEX NAME)

Absolute stereochemistry.

• HCl

380227-13-4 CAPLUS
1(2H)-Phthalazinone, 4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-2-(4-piperidinyl)-, monohydrochloride, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

• HCl

666735-60-0 CAPLUS

ANSWER 14 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

• HCl

666750-58-9 CAPLUS
3(2H)-Pyridazinone,
3-dihydro-7-methoxy-2,2-dimethyl-4-benzofuranyl)4,5-dihydro-2-(4-piperidinyl)-, monohydrochloride (9CI) (CA INDEX NAME)

HC1

REFERENCE COUNT: THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

WO 2003-EP1876

W 20030225

L4 ANSWER 15 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:719308 CAPLUS
DOCUMENT NUMBER: 139:240373
Pharmaceutical composition of a phosphodiesterase 4
historica

receptor antagonist for the treatment of respiratory diseases
Beume, Rolf; Bundschuh, Daniela; Weimar, Christian;
Wollin, Stefan-lutz
Altana Pharma Ag, Germany
PCT Int. Appl., 87 pp.
CODEN: PIXXD2 INVENTOR(S):

PATENT ASSIGNEE(S): SOURCE:

DOCUMENT TYPE: LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION.

English

PATENT	1	NPOR	MATI	ON:														
P	AT											LICA	TION	NO.		ם	ATE	
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W	0	2003	0740	55		A1		2003	0912		NO	2003	-EP1	876		2	0030	225
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E	P	1482	938			A1		2004	1208		EΡ	2003	-708	130		2	0030	225
		R:	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GF	, IT	, LI	, LU	, NL,	SE,	MC,	PT,
			İE,	SI,	LT.	LV.	PI.	MK,	CY.	AL,	TF	, BG	, CZ	, EE	, HU,	sk		
B	R	2003	0082	20		A		2005	0104		BR	2003	-822	0		2	0030	225
U	s	2005	1120	69		A1		2005	0526		US	2004	-506	875		2	0030	225
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		2004															0040	
		2004						2004									0041	
PRIORI	ΤY	APP	LN.	INPO	.:						EΡ	2002	-498	7		A 2	0020	306

The invention discloses the combined administration of PDE4 or PDE3/4 inhibitors and histamine receptor antagonists for the treatment of respiratory diseases.
449760-14-9 449760-15-0 449760-16-1
449760-17-2 449760-19-4 449760-20-7
449760-22-9 449760-23-0 449760-24-1
449760-25-2 449760-23-0 449760-24-1
449760-29-6 449760-10-9 449760-35-4
449760-40-1 449760-40-149760-35-4
449760-51-4 449760-40-49760-50-3
449760-51-4 449760-51-5
449760-51-4 596102-05-9
449760-51-4 596102-07-7 596102-09-9
RL: PAC (Phermacological activity); THU (Therapeutic use); BIOL

L4 ANSWER 15 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

449760-16-1 CAPLUS
Piperidine, 1-acetyl-4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1Rl)-phthalazinyll- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-17-2 CAPLUS
CN 1-Piperidinepentanoic acid,
4-[{4aS,8aR}-4-{3,4-diethoxyphenyl}-4a,5,8,8a-terahydro-1-oxo-2(1H)-phthalazinyl]-ō-oxo- {9CI} (CA INDEX NAME)

Absolute stereochemistry.

Absolute stereochemistry.

RN 449760-15-0 CAPLUS
CN Piperidine,
4-[(4aS,8aP.4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-(methylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 15 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

449760-19-4 CAPLUS
1-Piperidinecarboxamide, 4-[{4a5,8aR}-4-(3,4-diethoxyphenyl}-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

1-Piperidinecarboxamide, 4-{(4aS,8aR)-4-(3,4-diethoxypheny1)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalaziny1}-N-pheny1-(9CI) (CA INDEX NAME)

449760-22-9 CAPLUS
1-Piperidinecarboxamide, 4-[(4aR,8aS)-4-(2,3-dihydro-7-methoxy-2,2-

dimethyl-4-benzofuranyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N{1,1-dimethylethyl)-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

449760-23-0 CAPLUS
Piperidine, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1cxo-2(1H)-phthalazinyl]-1-[{5-(dimethylamino)-1-naphthalenyl}sulfonyl](9CI) (CA INDEX NAME)

Absolute stereochemistry.

ANSWER 15 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 449760-25-2 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(4pyridinylmethyl)-4-piperidinyl]-, (4aS,8aR)- (9CI) (CA INDEX NAME)

RN 449760-26-3 CAPLUS
CN Morpholine,
4-[[4-[(4aS, BaR)-4-[3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro1-0x0-2(lH)-phthalazinyl)-1-piperidinyl]carbonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 15 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

PAGE 1-A

PAGE 2-A

RN 449760-24-1 CAPLUS CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(4-nitrophenyl)-4-piperidinyl]-, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 15 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 449760-28-5 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(1methyl-1H-pyrazolo(3,4-d)pyrimidin-4-yl)-4-piperidinyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 2-A

449760-29-6 CAPLUS 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-(1-thieno[2,3-d]pyrimidin-4-yl-4-piperidinyl)-, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

PAGE 2-A

RN 449760-30-9 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(2-

ANSWER 15 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN NAME) (Continued)

Absolute stereochemistry.

449760-42-3 CAPLUS 2,3-Piperazinedione, 1-[[4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]carbonyl}-4-ethyl-(9CI) (CA INDEX NAME)

RN 449760-47-8 CAPLUS
CN Piperidine,
4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo2(1H)-phthalazinyl]-1-(4-pyridinylcarbonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

ANSWER 15 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued) pyrimidinyl)-4-piperidinyl]-, (4as,8ar)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-35-4 CAPLUS
CN Morpholine.
4-[[4-[[44.5,8aR]-4-(3,4-diethoxyphenyl]-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

449760-40-1 CAPLUS

1-Piperidineacetamide, 4-[(4as,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-(1-methylethyl)- (9C1) (CA INDEX

ANSWER 15 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

449760-48-9 CAPLUS 1(2H)-Phthalazinone, 2-(1-[2-(4-amino-3,5-dichlorophenyl)-2-oxoethyl]-4-piperidinyl)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-, (4a5,8aR)-(9CI) (CA INDEX NAME)

RN 449760-49-0 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-[(2oxo-2H-1-benzopyran-7-y1)methyl]-4-piperidinyl]-, [4aS,8aR]- (9CI) (CA
INDEX NAME)

RN 449760-50-3 CAPLUS
CN Morpholine,
4-[(4-[(485,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]acetyl}- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-51-4 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3, 4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(2-phenylethyl)-4-piperidinyl]-, (4aS,8aR)- (9CI) {CA INDEX NAME}

Absolute stereochemistry.

ANSWER 15 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 449760-56-9 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-[[4[1,2,3-thiadiazol-4-yl)phenyl]methyl]-4-piperidinyl]-, (4aS,8aR)- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

449760-57-0 CAPLUS
Benzoic acid, 4-[[(4-[(4as,8aR)-4-[3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(lH)-phthalarinyl)-1-piperidinyl]acetyl]amino]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 15 OF 22 CAPLUS COPYRIGHT 2007 ACS ON STN (Continued)

RN 449760-52-5 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-{3pyridinylmethyl)-4-piperidinyl]-, (4aS,8aR)- {9CI} (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-53-6 CAPLUS
CN 1(2H)-Phthalezinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(2-pyridinylmethyl)-4-piperidinyl]-, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

ANSWER 15 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

449760-58-1 CAPLUS
1-Piperidineactamide, 4-[(4a5,8aR)-4-(1,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

N 596102-01-1 CAPLUS N 1(2H)-Phthalarinone, -(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-{1-methylethyl)-4-piperidinyl]- (9CI) (CA INDEX NAME)

RN 596102-07-7 CAPLUS CN Piperidine, 4-{(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl}-1-(4-morpholinylacetyl)- (9CI) (CA IN (CA INDEX NAME)

Absolute stereochemistry.

RN 596102-09-9 CAPLUS
CN Piperidine,
4-[(4as,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo2(1H)-phthalazinyl]-1-[[4-[2-(dimethylamino)ethyl]-1-piperazinyl]acetyl](9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 16 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:832801 CAPLUS
DOCUMENT NUMBER: 137:337906
TITLE: Preparation of phthalazinones as phosphodiesterase

INVENTOR (5) :

inhibitors.
Hatzelmann, Armin; Marx, Degenhard; Steinhilber, Wolfram; Sterk, Geert Jan
Altana Pharma A.-G., Germany
PCT Int. Appl., 42 pp.
CODEN: PIXXD2
Patent
English
1

PATENT ASSIGNEE(S): SOURCE:

DOCUMENT TYPE: LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

	TENT I				V 7 177		D 1 1111					701			_		
	TENT																
WO	2002	0859	06		A2		2002	1031									
		AE, HU,	AL, ID,	AU, IL,	BA, IN,	BG, IS,	BR, JP,	CA, KR, US,	CN, LT,	LV,	MA,	MK,	MX,	NO,	NZ,	PH,	PL,
		AT,	BE, SE,	CH.				ES,			-						
	2445																
EP	1385																
	R: 2003 2003							FR, MK,									
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	1082							0930									
	2003																
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									,	WO 2	002-	EP44	38	1	W 2	0020	423

OTHER SOURCE(S):

MARPAT 137:337906

ANSWER 15 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

REFERENCE COUNT:

THERE ARE 6 CITED REPERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L4 ANSWER 16 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

AB Title compds. (I; Rl = alkoxy, fluoroalkoxy; R2 = F, Br, Cl; R3, R4 = H; R3R4 = bond; R5 = alkyl, cycloalkyl, cycloalkylmethyl, alkenyl, alkynyl, phenylalkenyl, polycycloalkyl, naphthyl, pyridyl, pyrazinyl, pyridazinyl, pyrimidinyl, etc.), were prepared Thus, cis-4-(3-chloro-4-methoxyphenyl)-2- piperidin-4-yl-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one (preparation given) was stirred 16 h with morpholine-4-carbonyl chloride in pyridine to give

cis-4-{3-chloro-4-methoxyphenyl})-2-[1-(1-morpholin-4-ylmethanoyl)piperidin-4-yl]-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one. The latter inhibited PDE4

and PDE7 with -log IC50 = 8.64 and 7.64, resp.
474122-96-8P 474122-97-9P 474122-98-0P
474122-99-1P 474123-17-6P 474123-26-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)

(Uses)
(Uses)
(preparation of phthalazinones as phosphodiesterase 4/7 inhibitors)
474122-96-8 CAPLUS
Morpholine, 4-[[4-[(4sR,8aS)-4-(3-chloro-4-methoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]carbonyl]-, rel- (9CI)
(CA INDEX NAME)

Relative stereochemistry.

RN 474122-97-9 CAPLUS
CN Piperidine,
-[1(4aR,885)-4-(3-chloro-4-methoxyphenyl)-4a,5,8,8a-tetrahydro1-oxo-2(1H)-phthalazinyl]-1-[(4-methylphenyl)sulfonyl]-, rel- [9CI) (CA INDEX NAME)

Relative stereochemistry.

474122-98-0 CAPLUS
Piperidine, 1-acetyl-4-[(4aR,8aS)-4-(3-chloro-4-methoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl}-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

474122-99-1 CAPLUS
1(2H)-Phthalazinone, 4-(3-chloro-4-methoxyphenyl)-4a,5,8,8a-tetrahydro-2[1-(4-pyridinylmethyl)-4-piperidinyl]-, (4aR,8aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

ANSWER 16 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

●x HCl

474123-18-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of phthalazinones as phosphodiesterase 4/7 inhibitors)
474123-18-7 CAPLUS
1(3H)-Phthalazinone, 4-(3-chloro-4-methoxyphenyl)-4a,5,8,8a-tetrahydro-2-(4-piperidinyl)-, (4aR,8aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

ANSWER 16 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 474123-17-6 CAPLUS
CN Piperidine,
4-[(48R,8aS)-4-(3-chloro-4-methoxyphenyl)-4a,5,8,8a-tetrahydro1-oxo-2(1H)-phthalazinyl]-1-[(2-oxo-1-imidazolidinyl)carbonyl]-, rel(9CI) (CA INDEX NAME)

Relative stereochemistry

474123-26-7 CAPLUS
1(2H)-Phthalazinone, 4-(3-chloro-4-methoxyphenyl)-4a,5,8,8a-tetrahydro-2[1-(4-pyridinylmethyl)-4-piperidinyl]-, hydrochloride, (4aR,8aS)-rel(SCI) (CA INDEX NAME)

Relative stereochemistry.

L4 ANSWER 17 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN ACCESSION NUMBER: 2002:637671 CAPLUS DOCUMENT NUMBER: 137:185496 TITILE: Preparation of piperidinyl benderivatives

Preparation of piperidinyl benzopyridazine

INVENTOR(S):

as PDE4 inhibitors for treatment of airway disorders Hatzelmann, Armin; Bundschuh, Daniela; Kley, Hans-peter; Timmerman, Hendrik; Christiasna, Johannes A. M.; Grundler, Gerhard; Gutterer, Beate; Sterk, Geert Jan Byk Gulden Lomberg Chemische Fabrik Gmbh, Germany PCT Int. Appl., 41 pp. CODEN: PIXXD2
PAtent
English

PATENT ASSIGNEE(S): SOURCE:

DOCUMENT TYPE: LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

		APPLICATION NO.	
		WO 2002-EP1547	
		CN, CO, CU, CZ, DZ, E	
		LT, LV, MA, MK, MX, N	
		VN, YU, ZA, ZW, AM, A	Z, BY, KG, KZ,
MD, RU, TJ,			
RW: AT, BE, CH,	CY, DE, DK, ES,	FI, FR, GB, GR, IE, I	T, LU, MC, NL,
PT, SE, TR			
CA 2438520	A1 20020822	CA 2002-2438520 EE 2003-311	20020214
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R: AT, BE, CH,	DE, DK, ES, FR,	GB, GR, IT, LI, LU, N	L, SE, MC, PT,
IE, SI, LT,	LV, FI, RO, MK,	CY, AL, TR	
HU 200303193	A2 , 20031229	CY, AL, TR HU 2003-3193 BR 2002-7278 JP 2002-564515 CN 2002-805038 NZ 2002-527424	20020214
BR 2002007278	A 20040210	BR 2002-7278	20020214
JP 2004518727	T 20040624	JP 2002-564515	20020214
CN 1524080	A 20040825	CN 2002-805038	20020214
NZ 527424	A 20050225	NZ 2002-527424	20020214
IN 2003MN00668	A 20050211	IN 2003-MN668	20030701
US 2004067946	A1 20040408	US 2003-467832	20030813
110 6953853	B2 20051011		
NO 2003003618	A 20031015	NO 2003-3618 BG 2003-108124 ZA 2003-6815 US 2005-143721 EP 2001-103496	20030814
BG 108124	A 20040831	BG 2003-108124	20030821
ZA 2003006815	A 20040617	ZA 2003-6815	20030901
US 2005234062	A1 20051020	US 2005-143721	20050603
RIORITY APPLN. INFO.:		EP 2001-103496	A 20010215
		US 2003-467832	A1 20030813

MARPAT 137:185496

Piperidinyl benzopyridazine derivs. [I; wherein R1 and R2 = H, or

her form an addnl. bond; R3 = substituted benzene, benzopyran derivative; R4

(C1-C4)alkoxy, optionally substituted with fluorine) were prepared (C1-C4)alkoxy, optionally substituted with tausians, and properties, to a solution of (4aS,8aR)-4-(3,4-diethoxyphenyl)-2-piperidin-4-yl-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one hydrochloride (synthetic preparation given) and p-TsCl in pyridine is stirred to give (4aS,8aR)-4-(3,4-diethoxyphenyl)-2-

p-Tscl in pyridine is stirred to give (448,8aR) -4-(3,4-diethoxyphenyl)-2[1-(toluene-4-sulfonyl)-piperidin-4-yl]-4a,5,8,8a-tetrahydro-2H-phthalazin1-one. The prepared compds. are effective PDE4 inhibitors useful in the
treatment of airway disorders.

1 49760-14-9P 449760-19-PP 449760-16-IP
449760-17-2P 449760-18-PP 449760-19-4P
449760-20-7P 449760-18-PP 449760-21-9P
449760-23-OP 449760-24-IP 449760-25-2P
449760-23-OP 449760-24-IP 449760-35-2P
449760-23-OP 449760-30-SP 449760-31-OP
449760-32-IP 449760-30-SP 449760-31-OP
449760-32-IP 449760-36-SP 449760-37-6P
449760-38-7P 449760-36-SP 449760-37-6P
449760-41-PP 449760-38-PP 449760-43-PP
449760-41-PP 449760-42-PP 449760-43-PP
449760-45-SP 449760-50-SP 449760-51-4P
449760-52-SP 449760-50-SP 449760-51-4P
449760-52-SP 449760-50-SP 449760-51-PP
A49760-58-IP
RLy PAC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of piperidinyl benzopyridazine derivs. as PDE4

(preparation of piperidinyl bei inhibitors for treatment of airway disorders) RN 449760-14-9 CAPLUS

ANSWER 17 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued) tetrahydro-1-oxo-2(1H)-phthalazinyl]- (9CI) (CA INDEX NAME)

449760-17-2 CAPLUS

CN 1-Piperidinepentanoic acid,
4-[(4as,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8atetrahydro-1-oxo-2(1H)-phthalazinyll-8-oxo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-18-3 CAPLUS
CN Piperidine,
-{(448,58R)-4-{3,4-diethoxyphenyl}-4a,5,8,8a-tetrahydro-1-oxo2(1H)-phthalazinyl}-1-(4-pyridinylcarbonyl)-, monohydrochloride (9CI)

INDEX NAME)

Absolute stereochemistry.

ANSMER 17 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
Piperidine,
4a5,8eR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo2(1H)-phthalazinyl)-1-[(4-methylphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-15-0 CAPLUS CN Piperidine, 4-[(4a5,8aR]-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-(methylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

449760-16-1 CAPLUS
Piperidine, 1-acetyl-4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-

ANSWER 17 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

449760-19-4 CAPLUS
1-Piperidinecarboxamide, 4-{(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalarinyl)-N-(1,1-dimethylethyl)- (9CI) (CA INDEX XAME)

Absolute stereochemistry.

449760-20-7 CAPLUS
1-Piperidinecarboxamide, 4-[(4as,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-terrahydro-1-oxo-2(1H)-phthalazinyl]-N-phenyl- (9CI) (CA INDEX NAME)

449760-21-8 CAPLUS
1-Piperidinecarboxamide, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

449760-22-9 CAPLUS 1-Piperidinecarboxamide, 4-{(4aR,8aS)-4-(2,3-dihydro-7-methoxy-2,2-

dimethyl-4-benzofuranyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-(1,1-dimethylethyl)-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

L4 ANSWER 17 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

PAGE 2-A

RN 449760-24-1 CAPLUS CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(4-nitrophenyl)-4-piperidinyl]-, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-25-2 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(4-pyridinylmethyl)-4-piperidinyl]-, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 17 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

449760-23-0 CAPLUS
Piperidine, 4-[(485,88R]-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-cxo-2(1H)-phthalazinyl}-1-[[5-(dimethylamino)-1-naphthalenyl]sulfonyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

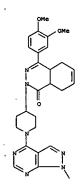
L4 ANSWER 17 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

N 449760-26-3 CAPLUS N Morpholine, -{[4-{(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]carbonyl}- (9CI) (CA INDEX NAME)

449760-27-4 CAPLUS
1(2H)-Phthalazinone, 2-(1-[2-(4-amino-3,5-dichlorophenyl)-2-oxoethyl]-4-piperidinyl]-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-,morohydrochloride, (4aS,8aR)- (9CI) (CA INDEX NAME)

RN 449760-28-5 CAPLUS
CN 1(2H)-Phthalazinone,
4(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-[1methyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)-4-piperidinyl]- (9CI) (CA INDEX NAME)

L4 ANSWER 17 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



PAGE 2-A

PAGE 1-A

449760-29-6 CAPLUS
1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-(1-thieno[2,3-d]pyrimidin-4-yl-4-piperidinyl)-, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 17 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

PAGE 1-A

RN 449760-30-9 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(2pyrimidinyl)-4-piperidinyl]-, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

(Continued) L4 ANSWER 17 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

RN 449760-31-0 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-{1-{2-oxo-2R-1-benzopyran-7-yl}methyl}-4-piperidinyl}-, monohydrochloride,
(4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

• HC1

RN 449760-32-1 CAPLUS
CN 1(2H)-Phthalasinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-(1-(1-methyl)-4-piperidinyl)-, monohydrochloride (9CI) (CA INDEX NAME)

Habte

L4 ANSWER 17 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

• HCl

RN . 449760-33-2 CAPLUS
CN Morpholine,
4-[[4-{(485,8aR)-4-(1,4-dimethoxyphenyl)-4s,5,8,8a-tetrahydro1-oxo-2(IH)-phthalazinyl]-1-piperidinyl]acetyl]-, monohydrochloride (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

RN 449760-34-3 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(2-phenylethyl)-4-piperidinyl)-, monohydrochloride, (4aS,8aR)- (9CI) (CA INDEX NAME)

ANSWER 17 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN INDEX NAME) (Continued)

Absolute stereochemistry.

●2 HCl

RN 449760-37-6 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-{2-pyridinylmethyl}-4-piperidinyl]-, dihydrochloride, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-38-7 CAPLUS
CN Morpholine,
4-[[4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-

Habte

L4 ANSWER 17 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN Absolute stereochemistry. (Continued)

● HCl

RN 449760-35-4 CAPLUS
CN Morpholine,
4-[[4-[(485,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1oxo-2(1H)-phthalazinyl]-1-piperidinyl]carbonyl}- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-36-5 CAPLUS CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(3-pyridinylmethyl)-4-piperidinyl)-, dihydrochloride, (4aS,8aR)- (9CI) (CA

ANSWER 17 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued) oxo-2(1H)-phthalazinyl]-1-piperidinyl]ectyl]-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-39-8 CAPLUS
CN 1-Piperazineethanamine,
4-[(4-[(485,88R)-4-(3,4-diethoxyphenyl)-4a,5,8,8atetrahydro-1-oxo-2(1H)-phthalazinyl)-1-piperidinyl]acetyl]-N,N-dimethyl-,
trihydrochloride (9CI) (CA INDEX NAME)

ANSWER 17 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

(Continued) PAGE 2-A

449760-40-1 CAPLUS
1-Piperidineacetamide, 4-{{4aS,8aR}-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl}-N-(1-methylethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-41-2 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4-8,5,8,8a-tetrahydro-2-[1-[4(1,2,3-thiadiazol-4-yl)phenyl)methyl)-4-piperidinyl}-, dihydrochloride,
(4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 17 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN Absolute stereochemistry. (Continued)

• HC1

449760-44-5 CAPLUS
1-Piperidineacetamide, 4-[(4as,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

● HC1

RN 449760-47-8 CAPLUS
CN Piperidine,
4-[(4a5,8a8)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo2(1H)-phthalarinyl}-1-(4-pyridinylcarbonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Habte

L4 ANSWER 17 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

●2 HC1

449760-42-3 CAPLUS 2,3-Piperazinedione, 1-[{4-[{4aS,8aR}-4-(3,4-dimethoxyphenyl]-4a,5,8,8a-tetrahydro-1-0xo-2(1H)-phthalazinyl]-1-piperidinyl]carbonyl}-4-ethyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

449760-43-4 CAPLUS
Benzoic acid, 4-[[[4-[(4aS,8aR)-4-[3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(IM)-phthalazinyl]-1-piperidinyl]acetyl]amino]-, ethyl ester, monohydrochloride (9CI) (CA INDEX NAME)

L4 ANSWER 17 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

449760-48-9 CAPLUS
1(2H)-Phthalazinone, 2-{1-{2-(4-amino-3,5-dichlorophenyl)-2-oxoethyl}-4-piperidinyl}-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-, (4aS,8aR)-(9CI) (CA INDEX NAME)

RN 449760-49-0 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-[(2-oxo-2R-1-benzopyran-7-yl)methyl]-4-piperidinyl]-, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

02/09/2007

RN 449760-50-3 CAPLUS
CN Morpholine,
4-[[4-(468,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro1-0x0-2(1H)-phthalazinyl]-1-piperidinyl]acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-51-4 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(2-phenylethyl)-4-piperidinyl]-, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 17 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

RN 449760-52-5 CAPLUS . CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(3-pyridinylmethyl)-4-piperidinyl]-, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-53-6 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(2pyridinylmethyl)-4-piperidinyl]-, (4eS,8aR)- (9CI) (CA INDEX NAME)

ANSWER 17 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 449760-54-7 CAPLUS
CN Morpholine,
4-[[4-[[48,8aR]-4-(3,4-diethoxyphenyl]-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-55-8 CAPLUS
CN 1-Piperazineethanamine,
4-[4-[48,8aR]-4-(3,4-diethoxyphenyl)-4a,5,8,8atetrahydro-1-oxo-2(1H)-phthalazinyl)-1-piperidinyl]acetyl}-N,N-dimethyl(9C1) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 17 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 449760-56-9 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-{1-[4-(1,2,3-thiadiazo1-4-y1)phenyl]methyl]-4-piperidinyl]-, (4aS,8aR)- (9CI)
(CA INDEX NAME) .

Absolute stereochemistry.

449760-57-0 CAPLUS
Benzoic acid, 4-{{[{4-{[(4a5,8aR)-4-{3,4-dimethoxyphenyl}-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl}-1-piperidinyl]acetyl]amino}-, ethylester (9CI) (CA INDEX NAME)

(Continued) L4 ANSWER 17 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

449760-58-1 CAPLUS
1-Piperidineacetamide, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

IT 380226-97-1P 380227-12-3P 380227-13-4P
449760-45-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation of piperidinyl benzopyridazine derivs. as PDE4
inhibitors for
treatment of airway disorders)
RN 380226-97-1 CAPLUS

1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrshydro-2-(4piperidinyl)-, monohydrochloride, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

ANSWER 17 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

• HC1

RN 449760-45-6 CAPLUS
CN 1(2H)-Phthalazinone,
4-(2,3-dihydro-7-methoxy-2,2-dimethyl-4-benzofuranyl)4-(5,5,8,8a-tetrahydro-2-(4-piperidinyl)-, (4aR,8aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

REFERENCE COUNT:

THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

L4 ANSWER 17 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

● HCl

380227-12-3 CAPLUS

RN 380227-12-3 CAPLUS CN Piperidine, 1-(chloroacety1)-4-[(4aS,8aR)-4-(3,4-diethoxypheny1)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalaziny1}- (9CI) (CA INDEX NAME)

380227-13-4 CAPLUS
1(2H)-Phthalazinone, 4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-2-(4-piperidinyl)-, monohydrochloride, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 18 OF 22 CAPLUS COPYRIGHT 2007 ACS ON STN ACCESSION NUMBER: 2001:904118 CAPLUS DOCUMENT NUMBER: 136:37625 TITLE: Preparation of pyridazinones as

136:37625
Preparation of pyridazinones as β2-adrenoreceptor agonists and PDE4 inhibitors
Hatzelmann, Armin; Bundschuh, Daniela; Eltze, INVENTOR(S): Manfrid;

Van der Laen, Yvonne; Timmermann, Hendrik; Christiaans, Johannes; Brundel, Paulus; Sterk, Geert Byk Gulden Lomberg Chemische Pabrik G.m.b.H.,

PATENT ASSIGNEE(S): Germany; Byk Nederland B.V. PCT Int. Appl., 79 pp. CODEN: PIXXD2 Patent English

SOURCE:

DOCUMENT TYPE: LANGUAGE:

LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

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OTHER SOURCE(S): MARPAT 136:37625

• STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT •

AB The title compds. [I; Arl = substituted Ph, dihydrobenzofuranyl; R6, R7 = H, alkyl; or R6 and R7 together and with inclusion of the two carbon atoms, to which they are bonded, form II-V; A = ChHZmYXChH2n, YXCmH2m2ChH2n; X = a bond, O, S, etc.; Y = a bond, phenylene, cycloalkylene, etc.; Z = 0, S, SO2, etc.; m = 0-4; n = 1-4; R8 = H, alkyl;

Ar2 = 8-hydroxy-IH-quinolin-2-on-5-yl, substituted Ph], useful as novel effective bronchial therapeutics, were prepared The general procedures

ANSWER 18 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued) prepn. of compds. I such as (cis)-VI.fumarate were described. Biol. data for compds. I were given.
380226-56-2P 380226-64-2P 380226-65-3P
380226-77-9P 380226-69-7P 380226-71-1P
380226-72-2P 380226-74-4P 380226-77-7P
380226-78-8P 380226-30-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyridszinones as β2-adrenoreceptor sqonists and PDF4

(Uase)
(preparation of pyridazinones as β2-adrenoreceptor agonists and PDE4
inhibitors)
380226-56-2 CAPEUS
Piperidine, 1-(4-[(2-(4-amino-3-chloro-5-cyanophenyl)-2hydroxyethyl)amino|-1-coxobutyl]-4-((48,582)-4-(3,4-dimethoxyphenyl)48,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl)-, (2E)-2-butenedioate

(salt) (9CI) (CA INDEX NAME)

CM 1

CRN 380226-55-1 CMF C34 H41 C1 N6 O5

Absolute stereochemistry.

CM 2

CRN 110-17-8 CMF C4 H4 O4

Double bond geometry as shown.

L4 ANSWER 18 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

hydroxyethyl]amino]propyl]-4-{(4as,8aR}-4-{3,4-dimethoxyphenyl}-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

380226-67-5 CAPLUS
Piperidine, 1-{[{2-{4-amino-3,5-dichlorophenyl}-2-hydroxyethyl]amino]acetyl]-4-{{485,8aR}-4-{3,4-diethoxyphenyl}-4a,5,8,8a-tetrahydro-1-oxo-2(IH)-phthalazinyl]-, {2E}-2-butenedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CRN 380226-66-4 CMP C33 H41 C12 N5 O5

Absolute stereochemistry.

L4 ANSWER 18 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

380226-64-2 CAPLUS
1(2H)-Phthalazinone, 2-[1-[2-[{2-[{2-(4-amino-3,5-dichlorophenyl)-2-hydroxyethyl]amino]ethyl]sulfonyl]lethyl]-4-piperidinyl]-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-, (4aS,8aR)-, (2E)-2-butenedioate (1:1) (aalt) (9CI) (CA INDEX NAME)

CRN 380226-63-1 CMF C33 H43 C12 N5 O6 S

CM 2

CRN 110-17-8 CMF C4 H4 O4

Double bond geometry as shown.

380226-65-3 CAPLUS
1-Piperidinecarbothioamide, N-[3-[[2-(4-amino-3,5-dichlorophenyl)-2-

L4 ANSWER 18 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

CM 2

Double bond geometry as shown

380226-69-7 CAPLUS
Piperidine, 1-[[2-[[2-(4-amino-3,5-dichlorophenyl)-2-hydroxyethyl]amino]ethyl]sulfonyl]-4-[(485,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-, (2E)-2-butenedioate

(malt) (9CI) (CA INDEX NAME)

CH 1

CRN 380226-68-6 CMP C31 H39 C12 N5 O6 S

CM 2

CRN 110-17-8 CMF C4 H4 O4

Double bond geometry as shown.

но2С Е СО2Н

380226-71-1 CAPLUS
Piperidine, 1-[(2S)-2-[(2-(3,4-diamino-5-chlorophenyl)-2hydroxyethyllamino]-1-oxopropyl]-4-[(48S,8aR]-4-(3,4-dimethoxyphenyl)4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl)-, (2E)-2-butenedioate

(salt) (9CI) (CA INDEX NAME)

CM 1

CRN 380226-70-0 CMF C32 H41 C1 N6 O5

Absolute stereochemistry.

ANSWER 18 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

380226-74-4 CAPLUS
Piperidine, 1-[3-[[2-[{2-(4-amino-3,5-dichlorophenyl)-2-hydroxyethyl]amino]ethyl]thio]-1-oxopropyl]-4-[(4a5,8aR)-4-(3,4-dimethoxyphenyl)-4-a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-,monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 2-A

L4 ANSWER 18 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

$$\begin{array}{c} \text{OMe} \\ \text{OMe} \\ \\ \text{H}_2\text{N} \\ \text{OH} \\ \end{array}$$

CM 2

Double bond geometry as shown.

но2С Е СО2Н

380226-72-2 CAPLUS
Piperidine, 4-[(4s5,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1oxo-2(1H)-phthalazinyl)-1-[(2-[(2-hydroxy-2-[4-hydroxy-3(hydroxymethyl)phenyl]ethyl]amino]ethyl}sulfonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 18 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

380226-77-7 CAPLUS
Piperidine, 1-[3-{(2-[[2-(4-amino-3-chloro-5-cyanophenyl)-2-hydroxyethyl]amino]ethyl]sulfonyl]-1-oxopropyl]-4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

380226-78-8 CAPLUS
Piperidine, 1-[{2S}-2-[[2-(4-amino-3-chloro-5-cyanophenyl}-2-hydroxyethyl]amino]-1-0xopropyl]-4-[(4aS, 8aR)-4-{3,4-dimethoxyphenyl}-4.5,8,8a-tetrahydro-1-0xo-2(1H)-phthalazinyl]-, monohydrochloride (9CI)(CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

Habte

● HC1

RN 380226-80-2 CAPLUS

RN Benzontrile, 2-amino-3-chloro-5-[2-[[6-[4-[4aS,8aR]-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl)-1-piperidinyllhexyl]amino|-1-hydroxyethyl]-, (2E)-2-butenedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 380226-79-9 CMF C36 H47 C1 N6 O4

Absolute stereochemistry.

CN 2

CRN 110-17-8

Double bond geometry as shown.

IT 380226-94-8P 380226-95-9P 380226-96-0P 380226-97-1P 380227-08-7P 380227-10-1P

L4 ANSWER 18 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
CN Carbamic acid, [4-{4-[(485,88R]-4-(3,4-dimethoxyphenyl)-4-5,8,8a-tetrahydro-1-oxo-2(IH)-phthalazinyl)-1-piperidinyl]-4-oxobutyl]-,
1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 380226-96-0 CAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4s,5,8,8a-tetrahydro-2-(4-piperidinyl)-, (4s5,8sR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 380226-97-1 CAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-(4-piperidinyl)-, monohydrochloride, (4aS,8aR)- (SCI) (CA INDEX NAME)

Absolute stereochemistry.

Habte

L4 ANSWER 18 OP 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
380247-11-3P 380227-12-3P 380227-13-4P
380247-14-5P 380227-13-9 380227-16-7P
380247-17-6P 380227-13-9P 380227-19-0P
380247-20-3P 380227-14-P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (prepn. of pyridazinones as β2-adrenoreceptor agonists and PDE4 inhibitors)
RN 380226-94-8 CAPLUS
CN Piperidine, 1-(4-amino-1-oxobutyl)-4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a.5,8,8a-tetrahydro-1-oxo-2(1H)-phthalezinyl]-, mono(trifluoroacetate)
CN 1
CRN 380226-93-7
CMF C25 H34 N4 O4

Absolute stereochemistry.

CM 2

CRN 76-05-1 CMP C2 H F3 O2

RN 380226-95-9 CAPLUS

L4 ANSWER 18 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continue

HC1

RN 380227-08-7 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxypheny)-2-[1-[2-(ethylsulfonyl)ethyl]4-piperidinyl]-4a,5,8,8a-tetrahydro-, (4a5,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

N 380227-10-1 CAPLUS
N 1-Piperidinecarbothioamide, N-(4-aminobutyl)-4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalarinyl]-, momo(trifluoroacetate) (9CI) (CA INDEX NAME)

CH

CRN 380227-09-8 CMP C26 H37 N5 03 S

02/09/2007

L4 ANSWER 18 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued) Absolute stereochemistry.

380227-11-2 CAPLUS Carbamic acid, [4-[[[4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-

tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]thioxomethyl]amino]buty 1]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME) Absolute stereochemistry.

L4 ANSWER 18 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

380227-14-5 CAPLUS
Piperidine, 4-(1(485,88R)-4-(3,4-dimethoxyphenyl)-4a,5,8,88-tetrahydro-1oxo-2(1R)-phthalazinyl)-1-(ethenylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

380227-15-6 CAPLUS
Piperidine, 1-[(2S)-2-amino-1-oxopropyl]-4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]- (9CI).
(CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 18 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 380227-12-3 CAPLUS '
CN Piperidine,
1-(chloroacetyl)-4-[(485,88R)-4-(3,4-diethoxyphenyl)-48,5,8,88tetrahydro-1-oxo-2(1H)-phthalazinyl)- (SCI) (CA INDEX NAME)

Absolute stereochemistry.

380227-13-4 CAPLUS
1(2H)-Phthalazinone, 4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-2-(4-piperidinyl)-, monohydrochloride, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 18 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

380227-16-7 CAPLUS
Piperidine, 4-{(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-

Ox0-2(1H)-phthalazinyl}-1-[(2S)-2-[[[(1,1-dimethylethyl)amino]carbonyl]ami
no]-1-oxopropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

380227-17-8 CAPLUS
Piperidine, 1-[3-[(2-aminoethyl)thio]-1-oxopropyl]-4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]- (9CI) (CA INDEX NAME)

380227-18-9 CAPLUS
Carbamic acid, [2-[[3-[4-[(4as,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]-3-oxopropyl)thio]ethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 38027-19-0 CAPLUS
CN Piperidine,
1-[3-[(2-mminoethyl)sulfonyl]-1-oxopropyl]-4-[(4a5,8aR)-4-(3,4- dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-,
monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

ANSWER 18 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

● HC1

380227-21-4 CAPLUS
1H-leoindole-1, 3(2H)-dione, 2-[6-[4-[(4as,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl)-1-piperidinyl]hexyl)-

(CA INDEX NAME)

Absolute stereochemistry.

REFERENCE COUNT:

THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

L4 ANSWER 18 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

(Continued)

PAGE 1-A

PAGE 2-A

● HC3

380227-20-3 CAPLUS
1(2H)-Phthalazinone, 2-{1-(6-aminohexyl)-4-piperidinyl]-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-, monohydrochloride, (4as,8aR)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 19 OF 22 CAPLUS COPYRIGHT 2007 ACS ON STN ACCESSION NUMBER: 2001:48306 CAPLUS DOCUMENT NUMBER: 134:266260 Studies on '--facile Studies on isocyanides and related compounds; a

synthesis of 4-phenyl-1-(2H)phthalazinone-2-alkanoic acid amides Marcaccini, Stefano; Pepino, Roberto; Polo, Cecilis; Pozo, Ma Cruz CNR, Centro di Studio sulla Chimica e la Struttura AUTHOR (S):

CORPORATE SOURCE:

CORPORATE SOURCE:

COMPOSTI Eterociclici e loro Applicazioni,
Dipartimento di Chimica Organica "Ugo Schiff",
Universita di Pirenze, Florence, 50121, Italy
SOURCE: Synthesis (2001), (1), 85-88
CODEN: SYNTBF; ISSN: 0039-7881
PUBLISHER: Georg Thieme Verlag
DOCURENT TYPE: Journal
LANGUAGE: English'
OTHER SOURCE(S): CASREACT 134:266260
AB A convenient synthesis of 4-phenyl-1-oxo-(2H)phthalazine-2-alkanoic amides
by the Ugi 4-component condensation (Ugi 4-CC) is reported. The reaction between acetaldehyde azine, 2-benzoylbenzoic acid, and cyclohexyl isocypanide spontaneously afforded N-cyclohexyl-2-(1,2-dihydro-1-oxo-4-phenylphthalazine-2-yl)propionamide upon elimination of McCHO from the intermediate Ugi 4-CC adduct. Starting from less reactive azines arising from Retones, the corresponding Ugi 4-CC adducts did not spontaneously cyclize, whereas phenylacetaldehyde azine afforded a mixture of the Ugi 4-CC

adduct and cyclized product. In all of the cases, the adducts were easily

IT

ly
cyclized in acidic medium.
3132049-47-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of oxophthalazinealkanoic amides)
312049-47-5 CAPUS
A-Pinaryiding-schownid.

333049-47-5 CAPLOS
4-Piperidinecarboxamide, 1-acetyl-N-cyclohexyl-4-(1-oxo-4-phenyl-2(1H)-phthalazinyl)- (9CI) (CA INDEX NAME)

REFERENCE COUNT:

28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR

RECORD. ALL CITATIONS AVAILABLE IN THE RE

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FORMAT

L4 ANSWER 20 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN OTHER SOURCE(S): MARPAT 129:136174 (Continued)

AB Title compds. [I; R1 = alkoxy, fluoroalkoxy; R2 = alkoxy, cycloalkoy, cycloalkylmethoxy, fluoroalkoxy; R3, R4 = H, or R3R4 = bond; R5 = R6, (CH2)mR7, (CH2)nCORS, CH(R9)2, (CH2)pAr; R6 = H, alkyl, cycloalkyl, cycloalkylmethyl, alkenyl, alkynyl, naphthyl, phenylalkenyl, pyridyl, pyrazinyl, indanyl, etc.; R7 = OH, halo, cyano, NO2, CNO2, CO2H, PhO, alkoxy, cycloalkoxy, alkylcarbonylamino, etc.; R8 = (substituted) Ph, naphthyl, phenanthryl, anthracenyl, R9 = (CH2)qPh; Ar = naphthyl, pyrazinyl, pyridazinyl, pyrimidinyl, quinazolinyl, cinnolinyl, isoquinolinyl, imidazolyl, pyrazolyl, oxazolyl, thiazolyl, turyl, thienyl, pyrrolyl, (substituted) Ph, etc.; m = 1-8; n = 1-4; p = 1-6; q = 0-2], were prepared Thus, cis-4-(3,4-dimethoxyphenyl)-2-propyl-4a,5,6,7,8,8a-hexahydro-2H-phthalazin-1-one (preparation outlined) inhibited PDE 4 with -log IC50 >7.5.

IT 210466-87-8P RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BSU (Biological)

(Biological study, unclassified); SFN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (preparation of srylphthalazinones as inhibitors of cyclic nucleotide phosphodiesterase)
RN 210466-87-8 CAPLUS
N 1(2H)-Phthalazinone.
4-(3,4-dimethoxyphenyl)-4a,5,6,7,8,8a-hexahydro-2-(1-methyl-4-piperidinyl)-, (4aR,8aS)-rel-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

Relative stereochemistry.

INVENTOR(S): Johanna;

Timmerman, Hendrik; Hatzelmann, Armin; Boss,
Hildegard; Hafner, Dietrich; Beume, Rolf; Kley,
Hans-Peter; Sterk, Geert Jan
Byk Gulden Lomberg Chemische Pabrik G.m.b.H., Germany
PCT Int. Appl., 59 pp.
CODEN: PIXXO2
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English
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PATENT ASSIGNEE (S) : SOURCE:

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L4 ANSWER 20 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

CM 2

Double bond geometry as shown.

REFERENCE COUNT:

THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

L4 ANSWER 21 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN ACCESSION NUMBER: 1961:76261 CAPLUS COPYRIGHT 2007 ACS on STN 1961:76261 CAPLUS SS:76261 CAPLUS SS:76261 CAPLUS SS:76261 CAPLUS SS:76261 CAPLUS SS:76261 CAPLUS FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE GB 858792 19610118 GB 1959-3664 15590202
Pyridezine derivs. showing slight toxicity and good analgetic action were prepared 1-Methyl-4-piperidylhydrazine (I) (55.6 g.) and 50 g. AccH2CHMeCO2H refluxed 19 hrs. in alc., the alc. removed, the residue dissolved in CHCl3, extracted with 2N HCl, made alkaline, extracted with CHC13, and

CMCIs, and concentrated gave
4.6-dimethyl-2-(1-methyl-4-piperidyl)-4.5-dihydro-3(2H)pyridazinone, m. 107-11*. This compound (10 g.) in 100 cc. AcOH
treated dropwise with 7.66 g. Br, the solvent removed at 100°, the
residue extracted from alkaline solution with CHCIs, and chromatographed

residue extracted from alkaline solution with CHCl3, and chromatographed on Al2O3
gave 4,6-dimethyl-2-(1-methyl-4-piperidyl)-3(2H)-pyridazinone, m.
87-9°; HBr salt m. 250-2°. Similarly, I and the appropriate
y-oxobutyric acids gave the following 2-(1-methyl-4-piperidyl)-3(2H)pyridazinones (substituents, m.p., and m.p. of 4,5-dihydro analog given):
6-Ph, 122-5° (HBr salt m. 310°), 153-5°, 4,6-Ph2,
142-3°, 138-60°; 4,6-Me2, - (HCl salt m. 252-4°),
92-4° (HCl salt m. 246-50°); 4,6-Meh, 284°,
124°; 6-(p-MeoC6H4), - (tartrate m. 199-200°),
107-8°; 6-(bromo-β-thienyl), - (HCl salt m. 266°),
103-5° (for 6-(β-thienyl) derivative); 4,5,6-Et2Ph, - (HCl salt m.
268-70°; HBr salt m. 262-4°), -; 4,6-PhMe, 140° (HCl
salt m. 228°), -; and 6,4-Ph(CN), 223° (HCl salt m.
280°), 183-5°. I (55.73 g.) in 200 cc. calc. added dropwise
at 15° to 37.15 g. Ac2O (II) in 200 cc. C6H6; the mixture kept
overnight, and refluxed 15 min., the solvent removed, and the residue
distilled in vacuo gave 2,3-butanedione
mono(1-methyl-4-piperidylhydrazone)
(IIII), bo.2 125-30°. NCM2CO2Et (11.3 g.), 16.4 g. III, 8.0 g.
AcOH, and 5.13 g. NH4OAc refluxed 17 hrs. in 100 cc. C6H6 with
H2O, concentrated at 50° in vacuo, the oil diluted with CHCl3, shaken

H2O, concentrated at 50° in vacuo, the oil diluted with CHCl3, shaken

with

2N NaOH, concentrated, and chromatographed on Al203 gave

4-cyano-5,6-dimethyl-2(1-methyl-4-piperidyl)-3(2H)-pyridazinone, m. 103-5° (Et20); HCl
salt m. 263-6°, HBr salt m. 238-5°. Similarly;
1,2-cyclohexanedione and I gave 1,2-cyclohexanedione mono(1-methyl-4piperidylhydrazone), b0.07 112-20°, and 4-cyano-5,6cyclotetramethylene-2-(1-methyl-4-piperidyl)-3(2H)-pyridazinone (HCl salt
m. 247-50°). 1-Isopropyl-4-piperidylhydrazine and II gave
2,3-butanedione mono(1-isopropyl-4-piperidylhydrazone), m. 84-7°,

ANSWER 21 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

860411-95-6 CAPLUS
4-Pyridazinecarbonitrile, 2,3,4,5-tetrahydro-2-(1-methyl-4-piperidyl)-3-oxo-6-phenyl- (6C1) (CA INDEX NAME)

ANSWER 21 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued) and 4-cyano-5,6-dimethyl-2-(1-isopropyl-4-piperidyl)-3(2H)-pyridazinone (hydrochloride m. 276-8°).
101268-89-7P, 3(2H)-Pyridazinone, 4,5-dihydro-2-(1-methyl-4-piperidyl)-6-phenyl-101599-83-1P, 3(2H)-Pyridazinone, 4,5-dihydro-4-methyl-2-(1-methyl-4-piperidyl)-6-phenyl-101599-90-0P, 3(2H)-Pyridazinone, 4,5-dihydro-6-(p-methoxyphenyl)-2-(1-methyl-4-piperidyl)-6-(he-diphenyl-86041)-95-6P, 4-Pyridazinecerbonitrile, 2,3,4,5-tetrahydro-2-(1-methyl-4-piperidyl)-1-cxo-6-phenyloxo-6-phenyl-RL: PREP (Preparation) (preparation of)
101268-89-7 CAPLUS
3(2H)-Pyridazinone, 4,5-dihydro-2-(1-methyl-4-piperidyl)-6-phenyl- (6CI)
(CA INDEX NAME)

RN 101599-83-1 CAPLUS CN 3(2H)-Pyridazinone, 4,5-dihydro-4-methyl-2-(1-methyl-4-piperidyl)-6-phenyl-(6CI) (CA INDEX NAME)

9-90-0 CAPLUS -Pyridazinone 101599-90-0 azinone, 4,5-dihydro-6-(p-methoxyphenyl)-2-(1-methyl-4-(6CI) (CA INDEX NAME)

102556-72-9 CAPLUS
3(2H)-Pyridazinone, 4,5-dihydro-2-(1-methyl-4-piperidyl)-4,6-diphenyl-(6CI) (CA INDEX NAME)

ANSWER 22 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN SSION NUMBER: 1960:118213 CAPLUS MENT NUMBER: 54:118213 INAL REPERENCE NO.: 54:22593b-i

ACCESSION NUMBER: DOCUMENT NUMBER: ORIGINAL REPERENCE NO.: TITLE:

OCCUMENT AUMBER: 94:11421

ORIGINAL REPERENCE No.: 54:22593b-1

TITLE: Synthetic drugs. V. Preparation of basically substituted 6-pyridazinones

AUTHOR(S): Jucker, E., Suess, R.

CORPORATE SOURCE: Sandoz, Basel, Switz.

SOURCE: Helvetica Chimica Acta (1959), 42, 2506-14

CODEN: HCACAV: ISSN: 0018-019X

Journal

ABC cf. preeding abstract Basically substituted pyridazinones were prepared by known methods. The already known 2-benzoylcyclohexane-1-carboxylic acid of m.p. 139-40° (Fieser and Novello, CA 36, 31715) was assigned the cis configuration; the epimeric trans derivative also was prepared Some of the

of the prepared compds. showed analgesic properties. To a cooled solution of KCN in water β-benzoylacrylic acid was added with stirring. The precipitated K salt was filtered off, dissolved in water and treated with 2N HCl to give 62% α-cyano-β-benzoylpropionic acid, separated as an oil, m. 101-3° (Et20). trans-2-Benzoylcyclohexane-1-carboxylic acid (I) was prepared in 92% yield, m. 151-2° (Et20) as described by F. and N. (loc. cit.) for the cis epimer (II). I also was obtained from II by heating a solution in 2N NaOH for 16 hrs. at 100°. II was refluxed with N-mathyl 4-piperidylhydrazine in EtOH for 24 hrs. to precipitate 74% cis-1-(1-mathyl-4-piperidyl)-1-phenyl-4,5-tetramethylen-4,5-dihydro-6-pyridazinone (III). m. 146° (EtOH); the trans epimer (IV) was prepared in an analogous way in 78% yield, m. 155° (EtOH). To a solution of IV in AcOH a solution of Br in AcOH was added dropwise. The mixture

mixture

was heated 2 hrs. to 120°, AcOH removed by distillation and the residue recrystd. from H2O and EtOH to give 62½

1-(1-methyl-4-piperidyl)-3-phenyl4,5-tetramethyl-ene-6-pyridazinone-HBr (V), m. 220-2°; the free base m. 179-80° (acetone). V was obtained from III in 69½ yield. The following 1-(1-methyl-4piperidyl)-6-pyridazinone derivs. were prepared in this way: 3-methyl, m. 87-9° (after sublimation at 80° in high vacuo; 3-phenyl, m. 122-5° (acetone) (HBr salt decomposing 310° (H2O)]; 3,5-dimethyl (HCl salt, m. 252-4° (EtOH);
3-methyl-5-phenyl, m. 140° (Et20-petr. ether); 3-phenyl-5-methyl (HCl salt hydrate), m. 284° (EtOH); 3-phenyl-5-cyano, m. 223° (EtOH) [KCl salt decomposing 380° (H2O)]; 3,5-diphenyl, m. 243° (acetone); 3-phenyl-4,5-diethyl (HCl salt hemihydrate), m. 268-70° (EtOH)]. The monohydratone from biacetyl and N-methyl-4-piperidylhydratine, Et cyanoacetate, AcOH, and NH4OAc were refluxed 15 hrs. in benzene while water was removed continuously. The benzene was distilled and the residue taken up in CHCl3. The solution was

cooled and shaken with 20% KOH, 18% HCl, and 2N HCl, resp., made alkaline with 18% KOH and again extracted with CHCl3. After removing the CHCl3, the

was taken up in Et20, petr. ether added, and the solution filtered through an Al203-column. The filtrate was treated with a 30% HBr-AcOH solution to

46.0 g. 1-(1-methyl-4-piperidyl)-3,4-dimethyl-5-cyano-6-pyridazinone-HBr

L4 ANSWER 22 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued) from 65.6 g. of the monohydrazone, decompg. 238-40° (MeOH-Et2O); free base m. 103-5° (Et2O). The following compds. were prepd. in this way: 1-(1-methyl-4-piperidyl)-3,4-tetramethylene-5-cyano-6-pyridazinone-HCl, decompg. 247-50° (EtOH-Et2O); 1-(1-isopropyl-4-piperidyl)3,4-dimethyl-5-cyano-6-pyridazinone-HCl, decompg. 276-68° (EtOH-Et2O), and 1-(1-methyl-2) dimethylaminoethyl)3,4-dimethyl-5-cyano-6-pyridazinone-HBr, m. 209-11° (EtOH).

17 879006-23-2P, 1(2H)-Phthalazinone, 4a,5,6,7,8,8a-hexahydro-2-(1-methyl-4-piperidyl)-4-phenyl-, trans-879006-25-4P, 1(2H)-Phthalazinone, 4a,5,6,7,8,8a-hexahydro-2-(1-methyl-4-piperidyl)-4-phenyl-, cis-RL: PREP (Preparation of)

RN 879006-23-2 CAPLUS
CN 1(2H)-Phthalazinone, 4a,5,6,7,8,8a-hexahydro-2-(1-methyl-4-piperidyl)-4-phenyl-, trans-(6CI) (CA INDEX NAME)

Relative stereochemistry.

879006-25-4 CAPLUS 1(2H)-Phthalazinone, 4a,5,6,7,8,8a-hexahydro-2-(1-methyl-4-piperidyl)-4-phenyl-, cie- (6CI) (CA INDEX NAME)

Relative stereochemistry.